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(54) Title: MULTIVARIANT IL-3 HEMATOPOIESIS FUSION PROTEIN			
(57) Abstract			
<p>The present invention relates to human interleukin-3 (hIL-3) variant or mutant proteins (muteins) fused with other colony stimulating factors (CSF), cytokines, lymphokines, interleukins, hematopoietic growth factors or IL-3 variants.</p>			

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**MULTIVARIANT IL-3 HEMATOPOIESIS
FUSION PROTEIN**

This is a continuation-in-part of United States Application Serial No. 08/192,325 filed February 04, 1994, which is incorporated herein by reference.

Field of the Invention

The present invention relates to fusion molecules composed of mutants or variants of human interleukin-3 (hIL-3) fused to a second colony stimulating factor (CSF) including cytokine, lymphokine, interleukin, hematopoietic growth factor or IL-3 variant with or without a linker.

15

Background of the Invention

Colony stimulating factors (CSFs) which stimulate the differentiation and/or proliferation of bone marrow cells have generated much interest because of their therapeutic potential for restoring depressed levels of hematopoietic stem cell-derived cells. CSFs in both human and murine systems have been identified and distinguished according to their activities. For example, granulocyte-CSF (G-CSF) and macrophage-CSF (M-CSF) stimulate the in vitro formation of neutrophilic granulocyte and macrophage colonies, respectively while GM-CSF and interleukin-3 (IL-3) have broader activities and stimulate the formation of both macrophage, neutrophilic and eosinophilic granulocyte colonies. IL-3 also stimulates the formation of mast, megakaryocyte and pure and mixed erythroid colonies.

Because of its ability to stimulate the proliferation of a number of different cell types and to support the growth and proliferation of progenitor cells, IL-3 has potential for therapeutic use in restoring hematopoietic cells to normal amounts in those cases where the number of cells has been reduced due to

diseases or to therapeutic treatments such as radiation and/or chemotherapy.

Interleukin-3 (IL-3) is a hematopoietic growth factor which has the property of being able to promote 5 the survival, growth and differentiation of hematopoietic cells. Among the biological properties of IL-3 are the ability (a) to support the growth and differentiation of progenitor cells committed to all, or virtually all, blood cell lineages; (b) to interact with early 10 multipotential stem cells; (c) to sustain the growth of pluripotent precursor cells; (d) to stimulate proliferation of chronic myelogenous leukemia (CML) cells; (e) to stimulate proliferation of mast cells, eosinophils and basophils; (f) to stimulate DNA synthesis 15 by human acute myelogenous leukemia (AML) cells; (g) to prime cells for production of leukotrienes and histamines; (h) to induce leukocyte chemotaxis; and (i) to induce cell surface molecules needed for leukocyte adhesion.

20 Mature human interleukin-3 (hIL-3) consists of 133 amino acids. It has one disulfide bridge and two potential glycosylation sites (Yang, et al., CELL 47:3 (1986)).

Murine IL-3 (mIL-3) was first identified by Ihle, et 25 al., J. IMMUNOL. 126:2184 (1981) as a factor which induced expression of a T cell associated enzyme, 20 - hydroxysteroid dehydrogenase. The factor was purified to homogeneity and shown to regulate the growth and differentiation of numerous subclasses of early 30 hematopoietic and lymphoid progenitor cells.

In 1984, cDNA clones coding for murine IL-3 were isolated (Fung, et al., NATURE 307:233 (1984) and Yokota, et al., PROC. NATL. ACAD. SCI. USA 81:1070 (1984)). The murine DNA sequence coded for a polypeptide of 166 amino acids including a putative signal peptide.

The gibbon IL-3 sequence was obtained using a gibbon cDNA expression library. The gibbon IL-3 sequence was

then used as a probe against a human genomic library to obtain a human IL-3 sequence.

Gibbon and human genomic DNA homologues of the murine IL-3 sequence were disclosed by Yang, et al., CELL 47:3 (1986). The human sequence reported by Yang, et al. included a serine residue at position 8 of the mature protein sequence. Following this finding, others reported isolation of Pro⁸ hIL-3 cDNAs having proline at position 8 of the protein sequence. Thus it appears that there may be two allelic forms of hIL-3.

Dorssers, et al., GENE 55:115 (1987), found a clone from a human cDNA library which hybridized with mIL-3. This hybridization was the result of the high degree of homology between the 3' noncoding regions of mIL-3 and hIL-3. This cDNA coded for an hIL-3 (Pro⁸) sequence.

U.S. 4,877,729 and U.S. 4,959,454 disclose human IL-3 and gibbon IL-3 cDNAs and the protein sequences for which they code. The hIL-3 disclosed has serine rather than proline at position 8 in the protein sequence.

Clark-Lewis, et al., SCIENCE 231:134 (1986) performed a functional analysis of murine IL-3 analogs synthesized with an automated peptide synthesizer. The authors concluded that the stable tertiary structure of the complete molecule was required for full activity. A study on the role of the disulfide bridges showed that replacement of all four cysteines by alanine gave a molecule with 1/500th the activity as the native molecule. Replacement of two of the four Cys residues by Ala(Cys⁷⁹, Cys¹⁴⁰ -> Ala⁷⁹, Ala¹⁴⁰) resulted in an increased activity. The authors concluded that in murine IL-3 a single disulfide bridge is required between cysteines 17 and 80 to get biological activity that approximates physiological levels and that this structure probably stabilizes the tertiary structure of the protein to give a conformation that is optimal for function. (Clark-Lewis, et al., PROC. NATL. ACAD. SCI. USA 85:7897 (1988)).

International Patent Application (PCT) WO 88/00598 discloses gibbon- and human-like hIL-3. The hIL-3 contains a Ser⁸ -> Pro⁸ replacement. Suggestions are made to replace Cys by Ser, thereby breaking the disulfide bridge, and to replace one or more amino acids at the glycosylation sites.

EP-A-0275598 (WO 88/04691) illustrates that Alal can be deleted while retaining biological activity. Some mutant hIL-3 sequences are provided, e.g., two double mutants, Alal -> Asp¹, Trp¹³ -> Arg¹³ (pGB/IL-302) and Alal -> Asp¹, Met³ -> Thr³ (pGB/IL-304) and one triple mutant Alal -> Asp¹, Leu⁹ -> Pro⁹, Trp¹³ -> Arg¹³ (pGB/IL-303).

WO 88/05469 describes how deglycosylation mutants can be obtained and suggests mutants of Arg⁵⁴Arg⁵⁵ and Arg¹⁰⁸Arg¹⁰⁹Lys¹¹⁰ might avoid proteolysis upon expression in Saccharomyces cerevisiae by KEX2 protease. No mutated proteins are disclosed. Glycosylation and the KEX2 protease activity are only important, in this context, upon expression in yeast.

WO 88/06161 mentions various mutants which theoretically may be conformationally and antigenically neutral. The only actually performed mutations are Met² -> Ile² and Ile¹³¹ -> Leu¹³¹. It is not disclosed whether the contemplated neutralities were obtained for these two mutations.

WO 91/00350 discloses nonglycosylated hIL-3 analog proteins, for example, hIL-3 (Pro⁸Asp¹⁵Asp⁷⁰), Met³ rhUIL-3 (Pro⁸Asp¹⁵Asp⁷⁰), Thr⁴ rhUIL-3 (Pro⁸Asp¹⁵Asp⁷⁰) and Thr⁶ rhUIL-3 (Pro⁸Asp¹⁵Asp⁷⁰). It is said that these protein compositions do not exhibit certain adverse side effects associated with native hIL-3 such as urticaria resulting from infiltration of mast cells and lymphocytes into the dermis. The disclosed analog hIL-3 proteins may have N termini at Met³, Thr⁴, or Thr⁶.

WO 91/12874 discloses cysteine added variants (CAVs)

of IL-3 which have at least one Cys residue substituted for a naturally occurring amino acid residue.

U.S. 4,810,643 discloses the DNA sequence encoding human G-CSF.

5 WO 91/02754 discloses a fusion protein composed of GM-CSF and IL-3 which has increased biological activity compared to GM-CSF or IL-3 alone. Also disclosed are nonglycosylated IL-3 and GM-CSF analog proteins as components of the fusion.

10 WO 92/04455 discloses fusion proteins composed of IL-3 fused to a lymphokine selected from the group consisting of IL-3, IL-6, IL-7, IL-9, IL-11, EPO and G-CSF.

15

Summary of the Invention

The present invention encompasses recombinant human interleukin-3 (hIL-3) variant or mutant proteins (muteins) fused to a second colony stimulating factor (CSF) include, cytokine, lymphokine, interleukin, hematopoietic growth factor (herein collectively referred to as "colony stimulating factors") or IL-3 variant with or without a linker. These hIL-3 muteins contain amino acid substitutions and may also have amino acid deletions at either/or both the N- and C- termini. This invention encompasses mixed function colony stimulating factors formed from covalently linked polypeptides, each of which may act through a different and specific cell receptor to initiate complementary biological activities.

30 Novel compounds of this invention are represented by the formulas

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁ where R₁ is a hIL-3 variant which contains multiple amino acid substitutions and which may have portions of the hIL-3 molecule deleted, R₂ is an IL-3, IL-3 variant or CSF with a different but complementary activity. The R₁ polypeptide is fused either directly or through a linker segment to the R₂ polypeptide. Thus L represents a

chemical bond or polypeptide segment to which both R1 and R2 are fused. Preferably, these mutant IL-3 polypeptides of the present invention contain four or more amino acids which differ from the amino acids found at the
5 corresponding positions in the native hIL-3 polypeptide. The invention also relates to pharmaceutical compositions containing the fusion molecules, DNA coding for the fusion molecules, and methods for using the fusion molecules. Additionally, the present invention relates
10 to recombinant expression vectors comprising nucleotide sequences encoding the hIL-3 fusion molecules, related microbial expression systems, and processes for making the fusion molecules using the microbial expression systems.

15 These fusion molecules may be characterized by having the usual activity of both of the peptides forming the fusion molecule or it may be further characterized by having a biological or physiological activity greater than simply the additive function of the presence of IL-3
20 or the second colony stimulating factor alone. The fusion molecule may also unexpectedly provide an enhanced effect on the activity or an activity different from that expected by the presence of IL-3 or the second colony stimulating factor or IL-3 variant. The fusion molecule
25 may also have an improved activity profile which may include reduction of undesirable biological activities associated with native hIL-3.

The present invention also includes mutants of hIL-3 in which from 1 to 14 amino acids have been deleted from
30 the N-terminus and/or from 1 to 15 amino acids have been deleted from the C-terminus, containing multiple amino acid substitutions, to which a second colony stimulating factor or IL-3 variant has been fused. Preferred fusion molecules of the present invention are composed of hIL-3 variants in which amino acids 1 to 14 have been deleted
35 from the N-terminus, amino acids 126 to 133 have been deleted from the C-terminus, and contains from about four

to about twenty-six amino acid substitutions in the polypeptide sequence fused to second colony stimulating factor or IL-3 variant.

The present invention also provides fusion molecules which may function as IL-3 antagonists or as discrete antigenic fragments for the production of antibodies useful in immunoassay and immunotherapy protocols.

Antagonists of hIL-3 would be particularly useful in blocking the growth of certain cancer cells like AML, CML and certain types of B lymphoid cancers. Other conditions where antagonists would be useful include those in which certain blood cells are produced at abnormally high numbers or are being activated by endogenous ligands. Antagonists would effectively compete for ligands, presumably naturally occurring hemopoietins including and not limited to IL-3, GM-CSF and IL-5, which might trigger or augment the growth of cancer cells by virtue of their ability to bind to the IL-3 receptor complex while intrinsic activation properties of the ligand are diminished. IL-3, GM-CSF and/or IL-5 also play a role in certain asthmatic responses. An antagonist of the IL-3 receptor may have the utility in this disease by blocking receptor-mediated activation and recruitment of inflammatory cells.

In addition to the use of the fusion molecules of the present invention *in vivo*, it is envisioned that *in vitro* uses would include the ability to stimulate bone marrow and blood cell activation and growth before infusion into patients.

30

Brief Description of the Drawings

Figure 1 is the human IL-3 gene for *E. coli* expression (pMON5873), encoding the polypeptide sequence of natural (wild type) human IL-3 [SEQ ID NO:49], plus an initiator methionine, as expressed in *E. coli*, with the amino acids numbered from the N-terminus of the natural hIL-3.

Figure 3 is the construction of plasmids pMON13018 and pMON13021. The plasmid pMON13018 is an intermediate plasmid used to construct the plasmid pMON13021 which encodes the polypeptide fusion pMON13021.

5 Figure 3 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusion pMON3988.

Figure 4 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusions
10 pMON3987 and pMON26430, pMON3995 and pMON26415.

Figure 5 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusion pMON26425.

15 Figure 6 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusions pMON26406 and pMON26433.

Figure 7 is the bioactivity, as measured in the methylcellulose assay, of the polypeptide fusions pMON26431 and pMON26427.

20

Detailed Description of the Invention

The present invention encompasses recombinant human interleukin-3 (hIL-3) variants or mutant proteins
25 (muteins) fused to itself, IL-3 or a second colony-stimulating factor (CSF) including but not limited to cytokine, lymphokine, interleukin, hematopoietic growth factor or IL-3 variant with or without a linker. This invention encompasses mixed function colony stimulating factors formed from covalently linked polypeptides, each of which may act through a different and specific cell receptor to initiate complementary biological activities. Hematopoiesis requires a complex series of cellular events in which stem cells generate continuously into
30 large populations of maturing cells in all major lineages. There are currently at least 20 known regulators with hematopoietic proliferative activity.

Most of these proliferative regulators can stimulate one or another type of colony formation in vitro, the precise pattern of colony formation stimulated by each regulator is quite distinctive. No two regulators stimulate exactly the same pattern of colony formation, as evaluated by colony numbers or, more importantly, by the lineage and maturation pattern of the cells making up the developing colonies. Proliferative responses can most readily be analyzed in simplified in vitro culture systems. Three quite different parameters can be distinguished:

alteration in colony size, alteration in colony numbers and cell lineage. Two or more factors may act on the progenitor cell, inducing the formation of larger number of progeny thereby increasing the colony size. Two or more factors may allow increased number of progenitor cells to proliferate either because distinct subsets of progenitors cells exist that respond exclusively to one factor or because some progenitors require stimulation by two or more factors before being able to respond.

Activation of additional receptors on a cell by the use of two or more factors is likely to enhance the mitotic signal because of coalescence of initially differing signal pathways into a common final pathway reaching the nucleus (Metcalf, 1989). Other mechanisms could explain synergy. For example, if one signaling pathway is limited by an intermediate activation of an additional signaling pathway by a second factor may result in a superadditive response. In some cases, activation of one receptor type can induce a enhanced expression of other receptors (Metcalf, 1993). Two or more factors may result in a different pattern of cell lineages than from a single factor. The use of fusion molecules may have the potential clinical advantage resulting from a proliferative response that is not possible by any single factor.

Hematopoietic and other growth factors can be grouped in to two distinct families of related receptors:

(1) tyrosine kinase receptors, including those for epidermal growth factor, M-CSF (Sherr, 1990) and SCF (Yarden et al., 1987); and (2) hematopoietic receptors, not containing a tyrosine kinase domain, but exhibiting obvious homology in their extracellular domain (Bazan, 1990). Included in this later group are erythropoietin (EPO) (D'Andrea et al., 1989), GM-CSF (Gearing et al., 1989), IL-3 (Kitamura et al., 1991), G-CSF (Fukunaga et al., 1990), IL-4 (Harada et al., 1990), IL-5 ((Takaki et al., 1990), IL-6 (Yamasaki et al., 1988), IL-7 (Goodwin et al., 1990), LIF (Gearing et al., 1991) and IL-2 (Cosman et al., 1987). Most of the later group of receptors exists in high-affinity form as a heterodimers. After ligand binding, the specific α -chains become associated with at least one other receptor chain (β -chain, γ -chain). Many of these factors share a common receptor subunit. The α -chains for GM-CSF, IL-3 and IL-5 share the same β -chain (Kitamura et al., 1991 Takaki et al., 1991) and receptor complexes for IL-6, LIF and IL-11 share a common β -chain (gp130) (Taga et al., 1989; Gearing et al., 1992). The receptor complexes of IL-2, IL-4 and IL-7 share a common γ -chain (Kondo et al., 1993; Russell et al., 1993; Noguchi et al., 1993).

The use of multiple factors may also have potential advantage by lowering the demands placed on factor-producing cells and their induction systems. If there are limitations in the ability of a cell to produce a factor then by lowering the required concentrations of each of the factors by using them in combination may usefully reduce demands on the factor-producing cells. The use of multiple factors may lower the amount of the factors that would be needed, probably reducing the likelihood of adverse responses.

Novel compounds of this invention are represented by a formula selected from the group consisting of

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁

where R1 is a hIL-3 variant which contains multiple amino acid substitutions and which may have portions of the hIL-3 molecule deleted as is disclosed in co-pending United States Patent Application Serial number 5 PCT/US93/11197, R2 is IL-3, IL-3 variant or a colony stimulating factor with a different but complementary activity. By complementary activity is meant activity which enhances or changes the response to another cell modulator. The R1 polypeptide is fused either directly or 10 through a linker segment to the R2 polypeptide. The term "directly" defines fusions in which the polypeptides are joined without a peptide linker. Thus L represents a chemical bound or polypeptide segment to which both R1 and R2 are fused in frame, most commonly L is a linear 15 peptide to which R1 and R2 are bound by amide bonds linking the carboxy terminus of R1 to the amino terminus of L and carboxy terminus of L to the amino terminus of R2. By "fused in frame" is meant that there is no translation termination or disruption between the reading 20 frames of R1 and R2. A nonexclusive list of other growth factors, colony stimulating factors (CSFs), cytokine, lymphokine, interleukin, hematopoietic growth factor within the definition of R2, which can be fused to a hIL-3 variant of the present invention include GM-CSF, CSF-1, 25 G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil 30 differentiation factor and stem cell factor (SCF) also known as steel factor or c-kit ligand. Additionally, this invention encompasses the use of modified R2 molecules or mutated or modified DNA sequences encoding these R2 molecules. The present invention also includes fusion 35 molecules in which R2 is a hIL-3 variant which means an IL-3 in which has amino acid substitutions and which may have portions of the hIL-3 molecule deleted such as what

is disclosed in PCT/US93/11197 and PCT/US93/11198 as well as other variants known in the art.

The linking group (L) is generally a polypeptide of between 1 and 500 amino acids in length. The linkers joining the two molecules are preferably designed to (1) allow the two molecules to fold and act independently of each other, (2) not have a propensity for developing an ordered secondary structure which could interfere with the functional domains of the two proteins, (3) have minimal hydrophobic or charged characteristic which could interact with the functional protein domains and (4) provide steric separation of R1 and R2 such that R1 and R2 could interact simultaneously with their corresponding receptors on a single cell. Typically surface amino acids in flexible protein regions include Gly, Asn and Ser. Virtually any permutation of amino acid sequences containing Gly, Asn and Ser would be expected to satisfy the above criteria for a linker sequence. Other neutral amino acids, such as Thr and Ala, may also be used in the linker sequence. Additional amino acids may also be included in the linkers due to the addition of unique restriction sites in the linker sequence to facilitate construction of the fusions.

Preferred linkers of the present invention include sequences selected from the group of formulas: (Gly₃Ser)_n, (Gly₄Ser)_n, (Gly₅Ser)_n, (Gly_nSer)_n or (AlaGlySer)_n.

One example of a highly-flexible linker is the (GlySer)-rich spacer region present within the pIII protein of the filamentous bacteriophages, e.g. bacteriophages M13 or fd (Schaller et al., 1975). This region provides a long, flexible spacer region between two domains of the pIII surface protein. The spacer region consists of the amino acid sequence:

GlyGlyGlySerGlyGlyGlySerGlyGlyGlySerGluGlyGlyGlySerGlu
GlyGlyGlySerGluGlyGlyGlySerGluGlyGlyGlySerGlyGlyGlySer

[SEQ ID NO:50]

The present invention also includes linkers in which an endopeptidase recognition sequence is included. Such a cleavage site may be valuable to separate the individual components of the fusion to determine if they are properly folded and active in vitro. Examples of various endopeptidases include, but are not limited to, Plasmin, Enterokinase, Kallikrein, Urokinase, Tissue Plasminogen activator, clostripain, Chymosin, Collagenase, Russell's Viper Venom Protease, Postproline cleavage enzyme, v8 protease, Thrombin and factor Xa.

Peptide linker segments from the hinge region of heavy chain immunoglobulins IgG, IgA, IgM, IgD or IgE provide an angular relationship between the attached polypeptides. Especially useful are those hinge regions where the cysteines are replaced with serines. Preferred linkers of the present invention include sequences derived from murine IgG gamma 2b hinge region in which the cysteins have been changed to serines. These linkers may also include an endopeptidase cleavage site. Examples of such linkers include the following sequences selected from the group of sequences

IleSerGluProSerGlyProIleSerThrIleAsnProSerProProSerLys
GluSerHisLysSerPro [SEQ ID NO:51]

IleGluGlyArgIleSerGluProSerGlyProIleSerThrIleAsnProSer
ProProSerLysGluSerHisLysSerPro [SEQ ID NO:52]

The present invention is, however, not limited by the form, size or number of linker sequences employed and the only requirement of the linker is that functionally it does not interfere adversely with the folding and function of the individual molecules of the fusion.

An alternative method for connecting two hematopoietic growth factors is by means of a non-covalent interaction. Such complexed proteins can be described by one the formulae:

R1-C1 + R2-C2; or C1-R1 + C2-R2; C1-R1 + R2-C2; or C1-R1 + R2-C2.

- 5 where R1 is a hIL-3 variant which contains multiple amino acid substitutions and which may have portions of the hIL-3 molecule deleted, R2 is a colony stimulating factor with a different but complementary activity. A nonexclusive list of other growth hormones, colony 10 stimulating factors (CSFs), cytokine, lymphokine, interleukin, hematopoietic growth factor within the definition of R2, which can be fused to a hIL-3 variant of the present invention include GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M- 15 CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF) also known as steel 20 factor or c-kit ligand. Domains C1 and C2 are either identical or non-identical chemical structures, typically proteinaceous, which can form a non-covalent, specific association. Complexes between C1 and C2 result in a one-to-one stoichiometric relationship between R1 and R2 25 for each complex. Examples of domains which associate are "leucine zipper" domains of transcription factors, dimerization domains of bacterial transcription repressors and immunoglobulin constant domains. Covalent bonds link R1 and C1, and R2 and C2, respectively. As 30 indicated in the formulae, the domains C1 and C2 can be present either at the N-terminus or C-terminus of their corresponding hematopoietic growth factor (R). These multimerization domains (C1 and C2) include those derived from the bZIP family of proteins (Abel et al., 1989; 35 Landshulz et al., 1988; Pu et al., 1993; Kozarides et al., 1988) as well as multimerization domains of the helix-loop-helix family of proteins (Abel et al., 1989;

- Murre et al., 1989; Tapscott et al., 1988; Fisher et al., 1991). Preferred fusions of the present invention include colony stimulating factors dimerized by virtue of their incorporation as translational fusions the leucine zipper dimerization domains of the bZIP family proteins Fos and Jun. The leucine zipper domain of Jun is capable of interacting with identical domains. On the other hand, the leucine zipper domain of Fos interacts with the Jun leucine zipper domain, but does not interact with other Fos leucine zipper domains. Mixtures of Fos and Jun predominantly result in formation of Fos-Jun heterodimers. Consequently, when fused to colony stimulating factors, the Jun domain can be used to direct the formation of either homo or heterodimers.
- 15 Preferential formation of heterodimers can be achieved if one of the colony stimulating factor partner is engineered to possess the Jun leucine zipper domain while the other is engineered to possess the Fos zipper.
- Peptides may also be added to facilitate purification or identification of fusion proteins (e.g., poly-His). A highly antigenic peptide may also be added that would enable rapid assay and facile purification of the fusion protein by a specific monoclonal antibody.
- 20 The present invention relates to novel fusion molecules composed of novel variants of human interleukin-3 (hIL-3) in which amino acid substitutions have been made at four or more positions in amino acid sequence of the polypeptide fused to second colony stimulating factor or IL-3 variant. Preferred fusion molecules of the present invention are (15-125)hIL-3 deletion mutants which have deletions of amino acids 1 to 14 at the N-terminus and 126 to 133 at the C-terminus and which also have four or more amino acid substitutions in the polypeptide fused to second colony stimulating factor or IL-3 variant. The present invention includes mutant polypeptides comprising minimally amino acids residues 15 to 118 of hIL-3 with or without additional amino acid

16.

extensions to the N-terminus and/or C-terminus which further contain four or more amino acid substitutions in the amino acid sequence of the polypeptide fused to another colony stimulating factor or IL-3 variant.

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As used herein human interleukin-3 corresponds to the amino acid sequence (1-133) as depicted in Figure 1 and (15-125) hIL-3 corresponds to the 15 to 125 amino acid sequence of the hIL-3 polypeptide. Naturally occurring variants of hIL-3 polypeptide amino acids are also included in the present invention (for example, the allele in which proline rather than serine is at position 8 in the hIL-3 polypeptide sequence) as are variant hIL-3 molecules which are modified post-translationally (e.g. glycosylation).

"Mutant amino acid sequence," "mutant protein" or "mutant polypeptide" refers to a polypeptide having an amino acid sequence which varies from a native sequence or is encoded by a nucleotide sequence intentionally made variant from a native sequence. "Mutant protein," "variant protein" or "mutein" means a protein comprising a mutant amino acid sequence and includes polypeptides which differ from the amino acid sequence of native hIL-3 due to amino acid deletions, substitutions, or both. "Native sequence" refers to an amino acid or nucleic acid sequence which is identical to a wild-type or native form of a gene or protein.

Human IL-3 can be characterized by its ability to stimulate colony formation by human hematopoietic progenitor cells. The colonies formed include erythroid, granulocyte, megakaryocyte, granulocytic macrophages and mixtures thereof. Human IL-3 has demonstrated an ability to restore bone marrow function and peripheral blood cell populations to therapeutically beneficial levels in studies performed initially in primates and subsequently in humans (Gillio, A. P., et al. (1990); Ganser, A. et

al. (1990); Falk, S., et al. (1991). Additional activities of hIL-3 include the ability to stimulate leukocyte migration and chemotaxis; the ability to prime human leukocytes to produce high levels of inflammatory mediators like leukotrienes and histamine; the ability to induce cell surface expression of molecules needed for leukocyte adhesion; and the ability to trigger dermal inflammatory responses and fever. Many or all of these biological activities of hIL-3 involve signal transduction and high affinity receptor binding. Fusion molecules of the present invention may exhibit useful properties such as having similar or greater biological activity when compared to native hIL-3 or by having improved half-life or decreased adverse side effects, or a combination of these properties. They may also be useful as antagonists. Fusion molecules which have little or no activity when compared to native hIL-3 may still be useful as antagonists, as antigens for the production of antibodies for use in immunology or immunotherapy, as genetic probes or as intermediates used to construct other useful hIL-3 muteins.

The novel fusion molecules of the present invention will preferably have at least one biological property of human IL-3 and the other colony stimulating factor or IL-3 variant to which it is fused and may have more than one IL-3-like biological property, or an improved property, or a reduction in an undesirable biological property of human IL-3. Some mutant polypeptides of the present invention may also exhibit an improved side effect profile. For example, they may exhibit a decrease in leukotriene release or histamine release when compared to native hIL-3 or (15-125) hIL-3. Such hIL-3 or hIL-3-like biological properties may include one or more of the following biological characteristics and in vivo and in vitro activities.

One such property is the support of the growth and differentiation of progenitor cells committed to

erythroid, lymphoid, and myeloid lineages. For example, in a standard human bone marrow assay, an IL-3-like biological property is the stimulation of granulocytic type colonies, megakaryocytic type colonies,

- 5 monocyte/macrophage type colonies, and erythroid bursts. Other IL-3-like properties are the interaction with early multipotential stem cells, the sustaining of the growth of pluripotent precursor cells, the ability to stimulate chronic myelogenous leukemia (CML) cell proliferation,
10 the stimulation of proliferation of mast cells, the ability to support the growth of various factor-dependent cell lines, and the ability to trigger immature bone marrow cell progenitors. Other biological properties of IL-3 have been disclosed in the art. Human IL-3 also has
15 some biological activities which may in some cases be undesirable, for example the ability to stimulate leukotriene release and the ability to stimulate increased histamine synthesis in spleen and bone marrow cultures and in vivo.

- 20 Biological activity of hIL-3 and hIL-3 fusion proteins of the present invention is determined by DNA synthesis by human acute myelogenous leukemia cells (AML). The factor-dependent cell line AML 193 was adapted for use in testing biological activity. The
25 biological activity of hIL-3 and hIL-3 fusion proteins of the present invention is also determined by counting the colony forming units in a bone marrow assay.

- Other in vitro cell based assays may also be useful to determine the activity of the fusion molecules
30 depending on the colony stimulating factors that comprise the fusion. The following are examples of other useful assays.

- TF-1 proliferation assay: The TF-1 cell line was derived from bone marrow of a patient with erythroleukemia (Kitamura et al., 1989). TF-1 cells respond to IL-3, GM-CSF, EPO and IL-5.

32D proliferation assay: 32D is a murine IL-3 dependent cell line which does not respond to human IL-3 but does respond to human G-CSF which is not species restricted.
T1165 proliferation assay: T1165 cells are a IL-6 dependent murine cell line (Nordan et al., 1986) which respond to IL-6 and IL-11.

Human Plasma Clot meg-CSF Assay: Used to assay megakaryocyte colony formation activity (Mazur et al., 1981).

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One object of the present invention is to provide hIL-3 variant with four or more amino acid substitutions in the polypeptide sequence fused to a second colony stimulating factor or IL-3 variant, which have similar or improved biological activity in relation to native hIL-3 or the second colony stimulating factor or IL-3 variant.

The hIL-3 variant fusion molecules of the present invention may have hIL-3 or hIL-3-like activity. For example, they may possess one or more of the biological activities of native hIL-3 and may be useful in stimulating the production of hematopoietic cells by human or primate progenitor cells. The fusion molecules of the present invention and pharmaceutical compositions containing them may be useful in the treatment of conditions in which hematopoietic cell populations have been reduced or destroyed due to disease or to treatments such as radiation or chemotherapy. Pharmaceutical compositions containing fusion molecules of the present invention can be administered parenterally, intravenously, or subcutaneously.

Native hIL-3 possesses considerable inflammatory activity and has been shown to stimulate synthesis of the arachidonic acid metabolites LTC₄, LTD₄, and LTE₄; histamine synthesis and histamine release. Human clinical trials with native hIL-3 have documented inflammatory responses (Biesma, et al., BLOOD, 80:1141-1148 (1992) and Postmus, et al., J. CLIN. ONCOL.,

10:1131-1140 (1992)). A recent study indicates that leukotrienes are involved in IL-3 actions in vivo and may contribute significantly to the biological effects of IL-3 treatment (Denzlinger, C., et al., BLOOD, 81:2466-2470
5 (1993))

Some fusion molecules of the present invention may have an improved therapeutic profile as compared to native hIL-3. For example, some fusion molecules of the present invention may have a similar or more potent
10 growth factor activity relative to native hIL-3 without having a similar or corresponding increase in the stimulation of leukotriene or histamine. These fusion molecules would be expected to have a more favorable therapeutic profile since the amount of polypeptide which
15 needs to be given to achieve the desired growth factor activity (e. g. cell proliferation) would have a lesser leukotriene or histamine stimulating effect. In studies with native hIL-3, the stimulation of inflammatory factors has been an undesirable side effect of the
20 treatment. Reduction or elimination of the stimulation of mediators of inflammation would provide an advantage over the use of native hIL-3.

Novel fusion molecules of the present invention may also be useful as antagonists which block the hIL-3
25 receptor by binding specifically to it and preventing binding of the agonist.

One potential advantage of the novel fusion molecules of the present invention, particularly those which retain activity similar to or better than that of native hIL-3, is that it may be possible to use a smaller amount of the biologically active mitein to produce the desired therapeutic effect. This may make it possible to reduce the number of treatments necessary to produce the desired therapeutic effect. The use of smaller amounts
30 may also reduce the possibility of any potential antigenic effects or other possible undesirable side effects. For example, if a desired therapeutic effect
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- can be achieved with a smaller amount of polypeptide it may be possible to reduce or eliminate side effects associated with the administration of native hIL-3 such as the stimulation of leukotriene and/or histamine release.
- 5 The novel fusion molecules of the present invention may also be useful in the activation of stem cells or progenitors which have low receptor numbers.

The present invention also includes the DNA sequences which code for the fusion proteins, DNA sequences which are substantially similar and perform substantially the same function, and DNA sequences which differ from the DNAs encoding the fusion molecules of the invention only due to the degeneracy of the genetic code. Also included in the present invention are; the oligonucleotide intermediates used to construct the mutant DNAs; and the polypeptides coded for by these oligonucleotides. These polypeptides may be useful as antagonists or as antigenic fragments for the production of antibodies useful in immunoassay and immunotherapy protocols.

Compounds of this invention are preferably made by genetic engineering techniques now standard in the art [United States Patent 4,935,233 and Sambrook et al., "Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory (1989)]. One method of creating the preferred hIL-3 (15-125) mutant genes is cassette mutagenesis [Wells, et al. (1985)] in which a portion of the coding sequence of hIL-3 in a plasmid is replaced with synthetic oligonucleotides that encode the desired amino acid substitutions in a portion of the gene between two restriction sites. In a similar manner amino acid substitutions could be made in the full-length hIL-3 gene, or genes encoding variants of hIL-3 in which from 1 to 14 amino acids have been deleted from the N-terminus and/or from 1 to 15 amino acids have been deleted from the C-terminus. When properly assembled these oligonucleotides would encode hIL-3 variants with the

desired amino acid substitutions and/or deletions from the N-terminus and/or C-terminus. These and other mutations could be created by those skilled in the art by other mutagenesis methods including; oligonucleotide-directed mutagenesis [Zoller and Smith (1982, 1983, 1984), Smith (1985), Kunkel (1985), Taylor, et al. (1985), Deng and Nickoloff (1992)] or polymerase chain reaction (PCR) techniques [Saiki, (1985)].

Pairs of complementary synthetic oligonucleotides encoding the desired gene can be made and annealed to each other. The DNA sequence of the oligonucleotide would encode sequence for amino acids of desired gene with the exception of those substituted and/or deleted from the sequence.

Plasmid DNA can be treated with the chosen restriction endonucleases then ligated to the annealed oligonucleotides. The ligated mixtures can be used to transform competent JM101 cells to resistance to an appropriate antibiotic. Single colonies can be picked and the plasmid DNA examined by restriction analysis and/or DNA sequencing to identify plasmids with the desired genes.

Fusing of the DNA sequences of the hIL-3 variant with the DNA sequence of the other colony stimulating factor or IL-3 variant may be accomplished by the use of intermediate vectors. Alternatively one gene can be cloned directly into a vector containing the other gene. Linkers and adapters can be used for joining the DNA sequences, as well as replacing lost sequences, where a restriction site was internal to the region of interest. Thus genetic material (DNA) encoding one polypeptide, peptide linker, and the other polypeptide is inserted into a suitable expression vector which is used to transform bacteria, yeast, insect cell or mammalian cells. The transformed organism is grown and the protein isolated by standard techniques. The resulting product is therefore a new protein which has a hIL-3 variant joined

by a linker region to a second colony stimulating factor or IL-3 variant.

Another aspect of the present invention provides plasmid DNA vectors for use in the expression of these novel fusion molecules. These vectors contain the novel DNA sequences described above which code for the novel polypeptides of the invention. Appropriate vectors which can transform microorganisms capable of expressing the fusion molecules include expression vectors comprising nucleotide sequences coding for the fusion molecules joined to transcriptional and translational regulatory sequences which are selected according to the host cells used.

Vectors incorporating modified sequences as described above are included in the present invention and are useful in the production of the fusion polypeptides. The vector employed in the method also contains selected regulatory sequences in operative association with the DNA coding sequences of the invention and capable of directing the replication and expression thereof in selected host cells.

As another aspect of the present invention, there is provided a method for producing the novel fusion molecules. The method of the present invention involves culturing a suitable cell or cell line, which has been transformed with a vector containing a DNA sequence coding for expression of a novel hIL-3 variant fusion molecule. Suitable cells or cell lines may be bacterial cells. For example, the various strains of E. coli are well-known as host cells in the field of biotechnology. Examples of such strains include E. coli strains JM101 [Yanish-Perron, et al. (1985)] and MON105 [Obukowicz, et al. (1992)]. Also included in the present invention is the expression of the fusion protein utilizing a chromosomal expression vector for E. coli based on the bacteriophage Mu (Weinberg et al., 1993). Various strains of B. subtilis may also be employed in this

method. Many strains of yeast cells known to those skilled in the art are also available as host cells for expression of the polypeptides of the present invention. When expressed in the E. coli cytoplasm, the above-mentioned mutant hIL-3 variant fusion molecules of the present invention may also be constructed with Met-Ala- at the N-terminus so that upon expression the Met is cleaved off leaving Ala at the N-terminus. The fusion molecules of the present invention may include fusion polypeptides having Met-, Ala- or Met-Ala- attached to the N-terminus. When the fusion molecules are expressed in the cytoplasm of E. coli, polypeptides with and without Met attached to the N-terminus are obtained. The N-termini of proteins made in the cytoplasm of E. coli are affected by posttranslational processing by methionine aminopeptidase (Ben-Bassat et al., 1987) and possibly by other peptidases. These mutant fusion molecules may also be expressed in E. coli by fusing a signal peptide to the N-terminus. This signal peptide is cleaved from the polypeptide as part of the secretion process. Secretion in E. coli can be used to obtain the correct amino acid at the N-terminus (e.g., Asn15 in the (15-125) hIL-3 polypeptide) due to the precise nature of the signal peptidase. This is in contrast to the heterogeneity often observed at the N-terminus of proteins expressed in the cytoplasm in E. coli.

Also suitable for use in the present invention are mammalian cells, such as Chinese hamster ovary cells (CHO). General methods for expression of foreign genes in mammalian cells are reviewed in: Kaufman, R. J. (1987) High level production of proteins in mammalian cells, in Genetic Engineering, Principles and Methods, Vol. 9, J. K. Setlow, editor, Plenum Press, New York. An expression vector is constructed in which a strong promoter capable of functioning in mammalian cells drives transcription of a eukaryotic secretion signal peptide coding region, which is translationally fused to the coding region for

the fusion molecule. For example, plasmids such as pCDNA I/Neo, pRC/RSV, and pRC/CMV (obtained from Invitrogen Corp., San Diego, California) can be used. The eukaryotic secretion signal peptide coding region can be 5 from the hIL-3 gene itself or it can be from another secreted mammalian protein (Bayne, M. L. et al. (1987) Proc. Natl. Acad. Sci. USA 84, 2638-2642). After construction of the vector containing the hIL-3 variant 10 gene, the vector DNA is transfected into mammalian cells. Such cells can be, for example, the COS7, HeLa, BHK, CHO, or mouse L lines. The cells can be cultured, for example, in DMEM media (JRH Scientific). The hIL-3 variant secreted into the media can be recovered by standard biochemical approaches following transient 15 expression 24 - 72 hours after transfection of the cells or after establishment of stable cell lines following selection for neomycin resistance. The selection of suitable mammalian host cells and methods for transformation, culture, amplification, screening and 20 product production and purification are known in the art. See, e.g., Gething and Sambrook, Nature, 293:620-625 (1981), or alternatively, Kaufman et al., Mol. Cell. Biol., 5(7):1750-1759 (1985) or Howley et al., U.S. Pat. No. 4,419,446. Another suitable mammalian cell line is 25 the monkey COS-1 cell line. A similarly useful mammalian cell line is the CV-1 cell line.

Where desired, insect cells may be utilized as host cells in the method of the present invention. See, e.g. Miller et al, Genetic Engineering, 8:277-298 (Plenum Press 1986) and references cited therein. In addition, general methods for expression of foreign genes in insect 30 cells using Baculovirus vectors are described in: Summers, M. D. and Smith, G. E. (1987) - A manual of methods for Baculovirus vectors and insect cell culture 35 procedures, Texas Agricultural Experiment Station Bulletin No. 1555. An expression vector is constructed comprising a Baculovirus transfer vector, in which a

strong Baculovirus promoter (such as the polyhedron promoter) drives transcription of a eukaryotic secretion signal peptide coding region, which is translationally fused to the coding region for the fusion polypeptide.

- 5 For example, the plasmid pVL1392 (obtained from Invitrogen Corp., San Diego, California) can be used. After construction of the vector carrying the gene encoding the fusion polypeptide, two micrograms of this DNA is cotransfected with one microgram of Baculovirus 10 DNA (see Summers & Smith, 1987) into insect cells, strain SF9. Pure recombinant Baculovirus carrying the fusion molecule is used to infect cells cultured, for example, in Excell 401 serum-free medium (JRH Biosciences, Lenexa, Kansas). The fusion molecule secreted into the medium 15 can be recovered by standard biochemical approaches. Supernatants from mammalian or insect cells expressing the fusion protein can be first concentrated using any of an number of commercial concentration units.

The fusion molecules of the present invention may be 20 useful in the treatment of diseases characterized by a decreased levels of either myeloid, erythroid, lymphoid, or megakaryocyte cells of the hematopoietic system or combinations thereof. In addition, they may be used to activate mature myeloid and/or lymphoid cells. Among 25 conditions susceptible to treatment with the polypeptides of the present invention is leukopenia, a reduction in the number of circulating leukocytes (white cells) in the peripheral blood. Leukopenia may be induced by exposure to certain viruses or to radiation. It is often a side 30 effect of various forms of cancer therapy, e.g., exposure to chemotherapeutic drugs, radiation and of infection or hemorrhage. Therapeutic treatment of leukopenia with these fusion molecules of the present invention may avoid undesirable side effects caused by treatment with 35 presently available drugs.

The fusion molecules of the present invention may be useful in the treatment of neutropenia and, for example,

- in the treatment of such conditions as aplastic anemia, cyclic neutropenia, idiopathic neutropenia, Chediak-Higashi syndrome; systemic lupus erythematosus (SLE), leukemia, myelodysplastic syndrome and myelofibrosis.
- 5 The fusion molecule of the present invention may be useful in the treatment or prevention of thrombocytopenia. Currently the only therapy for thrombocytopenia is platelet transfusions which are costly and carry the significant risks of infection (HIV, 10 HBV) and alloimmunization. The fusion molecule may alleviate or diminish the need for platelet transfusions. Severe thrombocytopenia may result from genetic defects such as Fanconi's Anemia, Wiscott-Aldrich, or May-Hegglin syndromes. Acquired thrombocytopenia may result from 15 auto- or allo-antibodies as in Immune Thrombocytopenia Purpura, Systemic Lupus Erythematosus, hemolytic anemia, or fetal maternal incompatibility. In addition, splenomegaly, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, infection or 20 prosthetic heart valves may result in thrombocytopenia. Severe thrombocytopenia may also result from chemotherapy and/or radiation therapy or cancer. Thrombocytopenia may also result from marrow invasion by carcinoma, lymphoma, leukemia or fibrosis.
- 25 The fusion molecules of the present invention may be useful in the mobilization of hematopoietic progenitors and stem cells into peripheral blood. Peripheral blood derived progenitors have been shown to be effective in reconstituting patients in the setting of autologous 30 marrow transplantation. Hematopoietic growth factors including G-CSF and GM-CSF have been shown to enhance the number of circulating progenitors and stem cells in the peripheral blood. This has simplified the procedure for peripheral stem cell collection and dramatically 35 decreased the cost of the procedure by decreasing the number of pheresis required. The fusion molecule may be useful in mobilization of stem cells and further enhance

the efficacy of peripheral stem cell transplantation.

Another projected clinical use of growth factors has been in the in vitro activation of hematopoietic progenitors and stem cells for gene therapy. In order to have the gene of interest incorporated into the genome of the hematopoietic progenitor or stem cell one needs to stimulate cell division and DNA replication.

5 Hematopoietic stem cells cycle at a very low frequency which means that growth factors may be useful to promote 10 gene transduction and thereby enhance the clinical prospects for gene therapy.

Many drugs may cause bone marrow suppression or hematopoietic deficiencies. Examples of such drugs are AZT, DDI, alkylating agents and anti-metabolites used in 15 chemotherapy, antibiotics such as chloramphenicol, penicillin, gancyclovir, daunomycin and sulfa drugs, phenothiazines, tranquilizers such as meprobamate, analgesics such as aminopyrine and dipyrone, anti-convulsants such as phenytoin or carbamazepine, 20 antithyroids such as propylthiouracil and methimazole and diuretics. The fusion molecules of the present invention may be useful in preventing or treating the bone marrow suppression or hematopoietic deficiencies which often occur in patients treated with these drugs.

25 Hematopoietic deficiencies may also occur as a result of viral, microbial or parasitic infections and as a result of treatment for renal disease or renal failure, e.g., dialysis. The fusion molecules of the present invention may be useful in treating such hematopoietic 30 deficiency.

The treatment of hematopoietic deficiency may include administration of a pharmaceutical composition containing the fusion molecules to a patient. The fusion molecules of the present invention may also be useful for 35 the activation and amplification of hematopoietic precursor cells by treating these cells in vitro with the fusion proteins of the present invention prior to

injecting the cells into a patient.

Various immunodeficiencies e.g., in T and/or B lymphocytes, or immune disorders, e.g., rheumatoid arthritis, may also be beneficially affected by treatment with the fusion molecules of the present invention. Immunodeficiencies may be the result of viral infections e.g. HTLV1, HTLVII, HTLVIII, severe exposure to radiation, cancer therapy or the result of other medical treatment. The fusion molecules of the present invention may also be employed, alone or in combination with other hematopoietins, in the treatment of other blood cell deficiencies, including thrombocytopenia (platelet deficiency), or anemia. Other uses for these novel polypeptides are in the treatment of patients recovering from bone marrow transplants in vivo and ex vivo, and in the development of monoclonal and polyclonal antibodies generated by standard methods for diagnostic or therapeutic use.

Other aspects of the present invention are methods and therapeutic compositions for treating the conditions referred to above. Such compositions comprise a therapeutically effective amount of one or more of the fusion molecules of the present invention in a mixture with a pharmaceutically acceptable carrier. This composition can be administered either parenterally, intravenously or subcutaneously. When administered, the therapeutic composition for use in this invention is preferably in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such a parenterally acceptable protein solution, having due regard to pH, isotonicity, stability and the like, is within the skill of the art.

The dosage regimen involved in a method for treating the above-described conditions will be determined by the attending physician considering various factors which modify the action of drugs, e.g. the condition, body weight, sex and diet of the patient, the severity of any

infection, time of administration and other clinical factors. Generally, a daily regimen may be in the range of 0.2 - 150 µg/kg of fusion protein per kilogram of body weight. This dosage regimen is referenced to a standard level of biological activity which recognizes that native IL-3 generally possesses an EC₅₀ at or about 10 picoMolar to 100 picoMolar in the AML proliferation assay described herein. Therefore, dosages would be adjusted relative to the activity of a given fusion protein vs. the activity of native (reference) IL-3 and it would not be unreasonable to note that dosage regimens may include doses as low as 0.1 microgram and as high as 1 milligram per kilogram of body weight per day. In addition, there may exist specific circumstances where dosages of fusion molecule would be adjusted higher or lower than the range of 10 - 200 micrograms per kilogram of body weight.

These include co-administration with other colony stimulating factor or IL-3 variant or growth factors; co-administration with chemotherapeutic drugs and/or radiation; the use of glycosylated fusion protein; and various patient-related issues mentioned earlier in this section. As indicated above, the therapeutic method and compositions may also include co-administration with other human factors. A non-exclusive list of other appropriate hematopoietins, CSFs, cytokines, lymphokines, hematopoietic growth factors and interleukins for simultaneous or serial co-administration with the polypeptides of the present invention includes GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, B-cell growth factor, B-cell differentiation factor and eosinophil differentiation factor, stem cell factor (SCF) also known as steel factor or c-kit ligand, or combinations thereof. The dosage recited above would be adjusted to compensate for such additional components in the therapeutic composition.

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Progress of the treated patient can be monitored by periodic assessment of the hematological profile, e.g., differential cell count and the like.

The present invention is also directed to the following:

1. R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁

wherein R₁ is a human interleukin-3 mutant polypeptide of the formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15

15 Cys Xaa
 20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa Xaa
 35 40 45

20 Xaa
 50 55 60

Xaa
 25 65 70 75

Xaa
 80 85 90

30 Xaa
 95 100 105

Xaa Phe Xaa
 110 115 120

35 Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
 125 130

[SEQ ID NO:1]

wherein

Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or

5 Arg;

Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
Gln;Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or
Cys;10 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
Ala;Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
Gln, Asn, Thr, Ser or Val;Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp,
15 Asn, Gln, Leu, Val or Gly;Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
Phe, Leu, Ser, or Arg;Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or
Leu;20 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or
Trp;

Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;

25 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
Trp;

Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;

Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,
Leu, or Lys;30 Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or
Gln;Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
or Glu;

Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;

35 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
Thr, Arg, Ala, Phe, Ile or Met;

Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or

Val;

- Xaa at position 36 is Asp, Leu, or Val;
- Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;
- Xaa at position 38 is Asn, or Ala;
- 5 Xaa at position 40 is Leu, Trp, or Arg;
- Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro;
- Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala;
- 10 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg., Thr, Gly or Ser;
- Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro;
- Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
- 15 Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;
- Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
- Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His;
- 20 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;
- Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,
- 25 Ser, Ala, Ile, Val, His, Phe, Met or Gln;
- Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- 30 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or Met;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;
- Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- 35 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 57 is Asn or Gly;

Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg;

Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;

5 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;

Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;

Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, 10 or Val;

Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;

Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;

Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or 15 Ser;

Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;

Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;

20 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;

Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;

Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, 25 Gln, Trp, or Asn;

Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;

Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;

Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;

30 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;

Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;

Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;

35 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;

Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly,

or Asp;

Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
or Arg;

5 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
or Lys;

Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;

Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;

10 Xaa at position 85 is Leu, Asn, Val, or Gln;

Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 87 is Leu, Ser, Trp, or Gly;

Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
15 Asn, or Ser;

Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;

Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;

20 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;

Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;

Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
25 Lys, His, Ala, or Pro;

Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;

Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;

30 Xaa at position 98 is His, Ile, A., Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;

Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;

Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
35 Gln, or Pro;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;

- Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
Pro;
- Xaa at position 103 is Asp, or Ser;
- Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
5 Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;
- 10 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,
His, Ser, Ala or Pro;
- Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
or Gly;
- Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln,
15 His, Glu, Ser, Ala, or Trp;
- Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;
- Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser,
or Phe;
- Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
20 Asp, Lys, Leu, Ile, Val or Asn;
- Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or
Leu;
- Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His,
Thr, Trp, or Met;
- 25 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val,
Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or
Ile;
- Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or
Pro;
- 30 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
or Tyr;
- Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
or Arg;
- Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or
35 Gln;
- Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
or Gly;

37

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys;

Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

5. and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and wherein from 4 to 44 of the amino acids designated by Xaa
 10 are different from the corresponding amino acids of native (1-133) human interleukin-3;

2. The fusion protein of 1 wherein said human interleukin-3 mutant polypeptide is of the Formula:

15 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
 1 5 10 15

Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa Xaa
 20 25 30

20

Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa Xaa
 35 40 45

Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu Xaa
 25 50 55 60

Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile Glu
 65 70 75

30 Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr Ala
 80 85 90

Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa Xaa
 95 100 105

35

Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu Xaa
 110 115 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe

125

130

[SEQ ID NO:2]

5

wherein

Xaa at position 17 is Ser, Gly, Asp, Met, or Gln;

Xaa at position 18 is Asn, His, or Ile;

Xaa at position 19 is Met or Ile;

10 Xaa at position 21 is Asp or Glu;

Xaa at position 23 is Ile, Ala, Leu, or Gly;

Xaa at position 24 is Ile, Val, or Leu;

Xaa at position 25 is Thr, His, Gln, or Ala;

Xaa at position 26 is His or Ala;

15 Xaa at position 29 is Gln, Asn, or Val;

Xaa at position 30 is Pro, Gly, or Gln;

Xaa at position 31 is Pro, Asp, Gly, or Gln;

Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or
Glu;

20 Xaa at position 33 is Pro or Glu;

Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
Gln, Glu, Ile, Phe, Thr or Met;

Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val;

Xaa at position 37 is Phe, Ser, Pro, or Trp;

25 Xaa at position 38 is Asn or Ala;

Xaa at position 42 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
Leu, Met, Tyr or Arg;

Xaa at position 44 is Asp or Glu;

Xaa at position 45 is Gln, Val, Met, Leu, Thr, Ala, Asn,
Glu, Ser or Lys;

Xaa at position 46 is Asp, Phe, Ser, Thr, Ala, Asn Gln,
Glu, His, Ile, Lys, Tyr, Val or Cys;

Xaa at position 50 is Glu, Ala, Asn, Ser or Asp;

Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;

Xaa at position 54 is Arg or Ala;

Xaa at position 55 is Arg, Thr, Val, Leu, or Gly;

- Xaa at position 56 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val or Lys;
- Xaa at position 60 is Ala or Ser;
- Xaa at position 62 is Asn, Pro, Thr, or Ile;
- 5 Xaa at position 63 is Arg or Lys;
- Xaa at position 64 is Ala or Asn;
- Xaa at position 65 is Val or Thr;
- Xaa at position 66 is Lys or Arg;
- Xaa at position 67 is Ser, Phe, or His;
- 10 Xaa at position 68 is Leu, Ile, Phe, or His;
- Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
- Xaa at position 71 is Ala, Pro, or Arg;
- Xaa at position 72 is Ser, Glu, Arg, or Asp;
- 15 Xaa at position 73 is Ala or Leu;
- Xaa at position 76 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
- Xaa at position 77 is Ile or Leu;
- Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
20 Gly, or Asp;
- Xaa at position 80 is Asn, Gly, Glu, or Arg;
- Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
- Xaa at position 83 is Pro or Thr;
- 25 Xaa at position 85 is Leu or Val;
- Xaa at position 87 is Leu or Ser;
- Xaa at position 88 is Ala or Trp;
- Xaa at position 91 is Ala or Pro;
- Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or
30 Arg;
- Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn,
Phe, Ser or Thr;
- Xaa at position 96 is Pro or Tyr;
- Xaa at position 97 is Ile or Val;
- 35 Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Leu,
Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
- Xaa at position 99 is Ile, Leu, or Val;

- Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser;
Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Pro,
Asn, Ile, Leu or Tyr;
Xaa at position 104 is Trp or Leu;
- 5 Xaa at position 105 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
Leu, Lys, Ile, Asp, or His;
Xaa at position 106 is Glu or Gly;
Xaa at position 108 is Arg, Ala, or Ser;
Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
- 10 Xaa at position 112 is Thr, Val, or Gln;
Xaa at position 114 is Tyr or Trp;
Xaa at position 115 is Leu or Ala;
Xaa at position 116 is Lys, Thr, Val, Trp, Ser, Ala, His,
Met, Phe, Tyr or Ile;
- 15 Xaa at position 117 is Thr or Ser;
Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or
Gly;
- Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
20 His, Ile, Tyr, or Cys;
Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

and which can additionally have Met preceding the amino
25 acid in position 1; and wherein from 1 to 14 amino acids
can be deleted from the N-terminus and/or from 1 to 15
amino acids can be deleted from the C-terminus; and
wherein from 4 to 35 of the amino acids designated by Xaa
are different from the corresponding amino acids of
30 native (1-133) human interleukin-3.

3. The fusion protein of 2 wherein said human
interleukin-3 mutant polypeptide is of the Formula:

35 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
1 5 10 15

41

Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa
 20 25 30

Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa
 5 35 40 45

Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala
 50 55 60

10 Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu
 65 70 75

Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala
 80 85 90
 15

Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa
 95 100 105

Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa
 20 110 115 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
 125 130

[SEQ ID NO:3]
 25

wherein

Xaa at position 17 is Ser, Gly, Asp, or Gln;

Xaa at position 18 is Asn, His, or Ile;

Xaa at position 23 is Ile, Ala, Leu, or Gly;

30 Xaa at position 25 is Thr, His, or Gln;

Xaa at position 26 is His or Ala;

Xaa at position 29 is Gln or Asn;

Xaa at position 30 is Pro or Gly;

Xaa at position 32 is Leu, Arg, Asn, or Ala;

35 Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met;

Xaa at position 35 is Leu, Ala, Asn, or Pro;

- Xaa at position 38 is Asn or Ala;
- Xaa at position 42 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
Met, Tyr or Arg;
- Xaa at position 45 is Gln, Val, Met, Leu, Ala, Asn, Glu,
5 or Lys;
- Xaa at position 46 is Asp, Phe, Ser, Gln, Glu, His, Val
or Thr;
- Xaa at position 50 is Glu Asn, Ser or Asp;
- Xaa at position 51 is Asn, Arg, Pro, Thr, or His;
- 10 Xaa at position 55 is Arg, Leu, or Gly;
- Xaa at position 56 is Pro, Gly, Ser, Ala, Asn, Val, Leu
or
- Gln;
- Xaa at position 62 is Asn, Pro, or Thr;
- 15 Xaa at position 64 is Ala or Asn;
- Xaa at position 65 is Val or Thr;
- Xaa at position 67 is Ser or Phe;
- Xaa at position 68 is Leu or Phe;
- Xaa at position 69 is Gln, Ala, Glu, or Arg;
- 20 Xaa at position 76 is Ser, Val, Asn, Pro, or Gly;
- Xaa at position 77 is Ile or Leu;
- Xaa at position 79 is Lys, Gly, Asn, Met, Arg, Ile, or
Gly;
- Xaa at position 80 is Asn, Gly, Glu, or Arg;
- 25 Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
His, Met, Phe, Ser, Thr, Tyr or Val;
- Xaa at position 87 is Leu or Ser;
- Xaa at position 88 is Ala or Trp;
- Xaa at position 91 is Ala or Pro;
- 30 Xaa at position 93 is Thr, Asp, or Ala;
- Xaa at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser
or
- Thr;
- Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu,
35 Lys, Met, Ser, Tyr, Val or Leu;
- Xaa at position 99 is Ile or Leu;
- Xaa at position 100 is Lys or Arg;

- Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Pro,
Asn, Ile, Leu or Tyr;
- Xaa at position 105 is Asn, Pro, Ser, Ile or Asp;
- Xaa at position 108 is Arg, Ala, or Ser;
- 5 Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
- Xaa at position 112 is Thr or Gln;
- Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, Tyr
or Ile;
- 8 Xaa at position 117 is Thr or Ser;
- 10 Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
- Xaa at position 121 is Ala, Ser, Ile, Pro, or Asp;
- Xaa at position 122 is Gln, Met, Trp, Phe, Pro, His, Ile,
or Tyr;
- Xaa at position 123 is Ala, Met, Glu, Ser, or Leu;

15

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and

20 wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133)human interleukin-3.

4. The fusion protein of 3 wherein said
25 human interleukin-3 mutant polypeptide is of the Formula:

- Xaa at position 42 is Gly, Asp, Ser, Ile, Leu, Met, Tyr,
or Ala;
- 30 Xaa at position 45 is Gln, Val, Met or Asn;
- Xaa at position 46 is Asp, Ser, Gln, His or Val;
- Xaa at position 50 is Glu or Asp;
- Xaa at position 51 is Asn, Pro or Thr;
- Xaa at position 62 is Asn or Pro;
- 35 Xaa at position 76 is Ser, or Pro;
- Xaa at position 82 is Leu, Trp, Asp, Asn Glu, His, Phe,
Ser or Tyr;

- Xaa at position 95 is His, Arg, Thr, Asn or Ser;
Xaa at position 98 is His, Ile, Leu, Ala, Gln, Lys, Met,
Ser, Tyr or Val;
Xaa at position 100 is Lys or Arg;
5 Xaa at position 101 is Asp, Pro, His, Asn, Ile or Leu;
Xaa at position 105 is Asn, or Pro;
Xaa at position 108 is Arg, Ala, or Ser;
Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, or
Tyr;
10 Xaa at position 121 is Ala, or Ile;
Xaa at position 122 is Gln, or Ile; and
Xaa at position 123 is Ala, Met or Glu.

6. A fusion protein having the formula
15 selected from the group consisting of

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁
wherein R₁ is a human interleukin-3 mutant
polypeptide of the Formula:

20

Asn Cys Xaa Xaa

1

5

10

15

25

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa

20

25

30

30

Xaa Xaa

35

40

45

35

Xaa Xaa

65

70

75

Xaa Xaa

80

85

90

Xaa Xaa Phe Xaa Xaa

95

100

105

5 Xaa Xaa Xaa Xaa Gln [SEQ ID NO:4]

110

wherein

- Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;
- 10 Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
- Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
- Xaa at position 6 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
- Xaa at position 7 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
- Gln, Asn, Thr, Ser or Val;
- 15 Xaa at position 8 is Glu, Trp, Pro, Ser, Ala, His, Asp,
- Asn, Gln, Leu, Val, or Gly;
- Xaa at position 9 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
- Phe, Leu, Ser, or Arg;
- Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or
- 20 Leu;
- Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or
- Ala;
- Xaa at position 12 is His, Thr, Phe, Gly, Arg, Ala, or
- Trp;
- 25 Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala;
- Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
- Trp;
- Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val;
- Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser,
- 30 Leu, or Lys;
- Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or
- Gln;
- Xaa at position 18 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
- or Glu;
- 35 Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu;
- Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
- Thr, Arg, Ala, Phe, Ile or Met;

- Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;
- Xaa at position 22 is Asp, Leu, or Val;
- Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile;
- 5 Xaa at position 24 is Asn, or Ala;
- Xaa at position 26 is Leu, Trp, or Arg;
- Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro;
- Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn, Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met;
- 10 Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly or Ser;
- Xaa at position 30 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala or Pro;
- Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr, 15 Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp;
- Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
- Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or His;
- 20 Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn;
- Xaa at position 35 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;
- Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, 25 Ser, Ala, Ile, Val, His, Phe, Met or Gln;
- Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr;
- 30 Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, Met, or;
- Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His, Ala or Leu;
- Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly;
- 35 Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 43 is Asn or Gly;

- Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- Xaa at position 45 is Glu, Tyr, His, Leu, Pro, or Arg;
- Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- 5 Xaa at position 47 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;
- Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, His, Pro,
10 or Val;
- Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or
15 Ser;
- Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or His;
- Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;
- 20 Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;
- Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;
- Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr,
Gln, Trp, or Asn;
- 25 Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;
- Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 30 Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu;
- Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp;
- Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu;
- 35 Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,

or Asp;

Xaa at position 66 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
or Arg;

Xaa at position 67 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
5 or Lys;

Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;

Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;

10 Xaa at position 71 is Leu, Asn, Val, or Gln;

Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 73 is Leu, Ser, Trp, or Gly;

Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His,
15 Asn, or Ser;

Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;

Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;

20 Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;

Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;

Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
25 Lys, His, Ala or Pro;

Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;

Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;

Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;

30 Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;

Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;

Xaa at position 86 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
35 Gln, Pro;

Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;

- Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- Xaa at position 89 is Asp, or Ser;
- Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
5 Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
Tyr, Leu, Lys, Ile, Asp, or His;
- Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;
- 10 Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,
His, Ser, Ala, or Pro;
- Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
or Gly;
- Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg,
15 His, Glu, Ser, Ala or Trp;
- Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;
- Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser,
or Phe;
- Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
20 Asp, Lys, Leu, Ile, Val or Asn;
- Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or
Leu;
- Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His,
Thr, Trp, or Met;
- 25 Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val,
Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or
Ile;
- Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or
Pro;
- 30 Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
or Tyr;
- Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
or Arg;
- Xaa at position 106 is Asn, Ala, Pro, Leu, His, Val, or
35 Gln;
- Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
or Gly;

50

Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

5

and which can additionally have Met- or Met-Ala- preceding the amino acid in position 1; and wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding native amino acids of
10 (1-133) human interleukin-3;

R₂ is a colony stimulating factor; and

L is a linker capable of linking R₁ to R₂.

15

The fusion protein of 5 wherein said human interleukin-3 mutant polypeptide is of the formula:

Asn Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa
20 1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa
20 25 30

25 Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu
35 40 45

Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile
50 55 60

30 Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr
65 70 75

Ala Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa
85 90

51

Xaa Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu

95

100

105

Xaa Xaa Xaa Xaa Gln Gln {SEQ ID NO:5}

5

110

wherein

- Xaa at position 3 is Ser, Gly, Asp, Met, or Gln;
Xaa at position 4 is Asn, His, or Ile;
10 Xaa at position 5 is Met or Ile;
Xaa at position 7 is Asp or Glu;
Xaa at position 9 is Ile, Ala, Leu, or Gly;
Xaa at position 10 is Ile, Val, or Leu;
Xaa at position 11 is Thr, His, Gln, or Ala;
15 Xaa at position 12 is His or Ala;
Xaa at position 15 is Gln, Asn, or Val;
Xaa at position 16 is Pro, Gly, or Gln;
Xaa at position 17 is Pro, Asp, Gly, or Gln;
Xaa at position 18 is Leu, Arg, Gln, Asn, Gly, Ala, or
20 Glu;
Xaa at position 19 is Pro or Glu;
Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
Gln, Glu, Ile, Phe, Thr or Met;
Xaa at position 21 is Leu, Ala, Asn, Pro, Gln, or Val;
25 Xaa at position 23 is Phe, Ser, Pro, or Trp;
Xaa at position 24 is Asn or Ala;
Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
Leu, Met Tyr or Arg;
Xaa at position 30 is Asp or Glu;
30 Xaa at position 31 is Gln, Val; Met, Leu, Thr, Ala, Asn,
Glu, Ser or Lys;
Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln,
Glu, His, Ile, Lys, Tyr, Val or Cys;
Xaa at position 36 is Glu, Ala, Asn, Ser or Asp;
35 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
Xaa at position 40 is Arg or Ala;

- Xaa at position 41 is Arg, Thr, Val, Leu, or Gly;
Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val Or Lys;
Xaa at position 46 is Ala or Ser;
- 5 Xaa at position 48 is Asn, Pro, Thr, or Ile;
Xaa at position 49 is Arg or Lys;
Xaa at position 50 is Ala or Asn;
Xaa at position 51 is Val or Thr;
Xaa at position 52 is Lys or Arg;
- 10 Xaa at position 53 is Ser, Phe, or His;
Xaa at position 54 is Leu, Ile, Phe, or His;
Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
- Xaa at position 57 is Ala, Pro, or Arg;
- 15 Xaa at position 58 is Ser, Glu, Arg, or Asp;
Xaa at position 59 is Ala or Leu;
Xaa at position 62 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
- Xaa at position 63 is Ile or Leu;
- 20 Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
Gly, or Asp;
Xaa at position 66 is Asn, Gly, Glu, or Arg;
Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
- 25 Xaa at position 69 is Pro or Thr;
Xaa at position 71 is Leu or Val;
Xaa at position 73 is Leu or Ser;
Xaa at position 74 is Ala or Trp;
Xaa at position 77 is Ala or Pro;
- 30 Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or
Arg;
Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn,
Phe, Ser or Thr;
- Xaa at position 82 is Pro or Tyr;
- 35 Xaa at position 83 is Ile or Val;
Xaa at position 84 is His, Ile, Asn, Leu, Ala, Thr, Leu,
Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;

- Xaa at position 85 is Ile, Leu, or Val;
 Xaa at position 86 is Lys, Arg, Ile, Gln, Pro, or Ser;
 Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Asn,
 Ile, Leu or Tyr;
- 5 Xaa at position 90 is Trp or Leu;
 Xaa at position 91 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
 Leu, Lys, Ile, Asp, or His;
 Xaa at position 92 is Glu, or Gly;
 Xaa at position 94 is Arg, Ala, or Ser;
- 10 Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
 Xaa at position 98 is Thr, Val, or Gln;
 Xaa at position 100 is Tyr or Trp;
 Xaa at position 101 is Leu or Ala;
 Xaa at position 102 is Lys, Thr, Val, Trp, Ser, Ala, His,
- 15 Met, Phe, Tyr or Ile;
 Xaa at position 103 is Thr or Ser;
 Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
 Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or
 Gly;
- 20 Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
 His, Ile, Tyr, or Cys;
 Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr,
 or Leu;
- 25 which can additionally have Met- or Met-Ala- preceding
 the amino acid in position 1; and wherein from 4 to 35 of
 the amino acids designated by Xaa are different from the
 corresponding amino acids of native human interleukin-3.

30 7. The fusion protein of 6 wherein said
 human interleukin-3 mutant polypeptide is of the Formula:

Asn	Cys	Xaa	Xaa	Met	Ile	Asp	Glu	Xaa	Ile	Xaa	Xaa	Leu	Lys	Xaa
1				5					10				15	

35

Xaa	Pro	Xaa	Pro	Xaa	Xaa	Asp	Phe	Xaa	Asn	Leu	Asn	Xaa	Glu	Asp
20								25					30	

54

Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu

35

40

45

5 Ala Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile

50

55

60

Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr

65

70

75

10

Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp

80

85

90

Xaa Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu

15

95

100

105

Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:6]

110

wherein

- 20 Xaa at position 3 is Ser, Gly, Asp, or Gln;
Xaa at position 4 is Asn, His, or Ile;
Xaa at position 9 is Ile, Ala, Leu, or Gly;
Xaa at position 11 is Thr, His, or Gln;
Xaa at position 12 is His or Ala;
- 25 Xaa at position 15 is Gln or Asn;
Xaa at position 16 is Pro or Gly;
Xaa at position 18 is Leu, Arg, Asn, or Ala;
Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
Ile, Phe, Thr or Met;
- 30 Xaa at position 21 is Leu, Ala, Asn, or Pro;
Xaa at position 24 is Asn or Ala;
Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
Met, Tyr or Arg;
- 35 Xaa at position 31 is Gln, Val, Met, Leu, Ala, Asn, Glu
or
Lys;
- Xaa at position 32 is Asp, Phe, Ser, Ala, Gln, Glu, His,

Val or Thr;

Xaa at position 36 is Glu, Asn, Ser or Asp;

Xaa at position 37 is Asn, Arg, Pro, Thr, or His;

Xaa at position 41 is Arg, Leu, or Gly;

- 5 Xaa at position 42 is Pro, Gly, Ser, Ala, Asn, Val, Leu or

Gln;

Xaa at position 43 is Asn, Pro, or Thr;

Xaa at position 50 is Ala or Asn;

- 10 Xaa at position 51 is Val or Thr;

Xaa at position 53 is Ser or Phe;

Xaa at position 54 is Leu or Phe;

Xaa at position 55 is Gln, Ala, Glu, or Arg;

Xaa at position 62 is Ser, Val, Asn, Pro, or Gly;

- 15 Xaa at position 63 is Ile or Leu;

Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly;

Xaa at position 66 is Asn, Gly, Glu, or Arg;

Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser, Thr, Tyr or Val;

- 20 Xaa at position 73 is Leu or Ser;

Xaa at position 74 is Ala or Trp;

Xaa at position 77 is Ala or Pro;

Xaa at position 79 is Thr, Asp, or Ala;

Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser or

Thr;

Xaa at position 84 is His, Ile, Asn, Ala, Thr, Arg, Gln, Glu, Lys, Met, Ser, Tyr, Val or Leu;

Xaa at position 85 is Ile or Leu;

- 30 Xaa at position 86 is Lys or Arg;

Xaa at position 87 is Asp, Pro, Met, Lys, His, Pro, Asn, Ile, Leu or Tyr;

Xaa at position 91 is Asn, Pro, Ser, Ile or Asp;

Xaa at position 94 is Arg, Ala, or Ser;

- 35 Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;

Xaa at position 98 is Thr or Gln;

Xaa at position 102 is Lys, Val, Trp, or Ile;

Xaa at position 103 is Thr, Ala, His, Phe, Tyr or Ser;
Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp;
Xaa at position 108 is Gln, Met, Trp, Phe, Pro, His, Ile,
5 or Tyr;
Xaa at position 109 is Ala, Met, Glu, Ser, or Leu;

and which can additionally have Met- or Met-Ala-
preceding the amino acid in position 1; and wherein from
10 4 to 26 of the amino acids designated by Xaa are
different from the corresponding amino acids of native
(1-133)human interleukin-3.

8. The fusion protein of 7 wherein said
15 human interleukin-3 mutant polypeptide is of the Formula:

Xaa at position 17 is Ser, Lys, Asp, Met, Gln, or Arg;
Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
Gln;
20 Xaa at position 19 is Met, Arg, Gly, Ala, or Cys;
Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
Ala;
Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, or
Val;
25 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, or
Gly;
Xaa at position 23 is Ile, Ala, Gly, Trp, Lys, Leu, Ser,
or Arg;
Xaa at position 24 is Ile, Gly, Arg, or Ser;
30 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
Xaa at position 26 is His, Thr, Phe, Gly, Ala, or Trp;
Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
Xaa at position 28 is Lys, Leu, Gln, Gly, Pro, Val or
35 Trp;
Xaa at position 29 is Gln, Asn, Pro, Arg, or Val;
Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,

- Leu; or Lys;
- Xaa at position 31 is Pro, Asp, Gly, Arg, Leu, or Gln;
- Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu;
- 5 Xaa at position 33 is Pro, Leu, Gln, Thr, or Glu;
- Xaa at position 34 is Leu, Gly, Ser, or Lys;
- Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, or Gln;
- Xaa at position 36 is Asp, Leu, or Val;
- Xaa at position 37 is Phe, Ser, or Pro;
- 10 Xaa at position 38 is Asn, or Ala;
- Xaa at position 40 is Leu, Trp, or Arg;
- Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, Pro;
- Xaa at position 42 is Gly, Asp, Ser, Cys, or Ala;
- Xaa at position 42 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
- 15 Cys, or Ser;
- Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, or Pro;
- Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, or Trp;
- 20 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, or Gly;
- Xaa at position 47 is Ile, Gly, Ser, Arg, Pro, or His;
- Xaa at position 48 is Leu, Ser, Cys, Arg, His, Phe, or Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
- 25 or Asp;
- Xaa at position 50 is Glu, Leu, Thr, Asp, or Tyr;
- Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;
- Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or
- 30 Thr;
- Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
- or Leu;
- 35 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, or Lys;
- Xaa at position 57 is Asn or Gly;

- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;
- Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
- Xaa at position 60 is Ala, Ser, Tyr, Asn, or Thr;
- 5 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, or Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Ser, Pro, or Val;
- 10 Xaa at position 64 is Ala, Asn, Ser, or Lys;
- Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- Xaa at position 66 is Lys, Ile, Val, Asn, Glu, or Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
- 15 Pro, or His;
- Xaa at position 68 is Leu, Val, Trp, Ser, Thr, or His;
- Xaa at position 69 is Gln, Ala, Pro, Thr, Arg, Trp, Gly, or Leu;
- Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 20 Xaa at position 71 is Ala, Met, Leu, Arg, Glu, Thr, Gln, Trp, or Asn;
- Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;
- Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,
- 25 or Arg;
- Xaa at position 74 is Ile, Thr, Pro, Arg, Gly, Ala;
- Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, or Leu;
- Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro,
- 30 Gly, or Asp;
- Xaa at position 77 is Ile, Ser, Arg, or Thr;
- Xaa at position 78 is Leu, Ala, Ser, Glu, Gly, or Arg;
- Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Ile, or Asp;
- 35 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, or Arg;
- Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, or

Lys;

- Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, or Asp;
Xaa at position 83 is Pro, Thr, Trp, Arg, or Met;
Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
5 Xaa at position 85 is Leu, Asn, or Gln;
Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
Xaa at position 87 is Leu, Ser, Trp, or Gly;
Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
10 or Asn;
Xaa at position 90 is Ala, Ser, Asp, Ile, or Met;
Xaa at position 91 is Ala, Ser, Thr, Phe, Leu, Asp, or
His;
Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, or
15 Leu;
Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, or
Pro;
20 Xaa at position 95 is His, Gln, Pro, Val, Leu, Thr or
Tyr;
Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
Xaa at position 97 is Ile, Lys, Ala, or Asn;
Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
25 or Pro;
Xaa at position 99 is Ile, Arg, Asp, Pro, Gln, Gly, Phe,
or His;
Xaa at position 100 is Lys, Tyr, Leu, His, Ile, Ser, Gln,
or Pro;
30 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, or Gln;
Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
Pro;
Xaa at position 103 is Asp, or Ser;
35 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;
Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,

60

- Tyr, Leu, Lys, Ile, or His;
 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
 or Pro;
 Xaa at position 108 is Arg, Asp, Leu, Thr, Ile, or Pro;
 5 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
 or Gly.

10 9. The fusion protein of 8 wherein said
 human interleukin-3 mutant polypeptide is of the Formula:

	1	5	10
	(Met) _m -Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr		
	15	20	
	Ser Trp Val Asn Cys Ser Xaa Xaa Xaa Asp Glu Ile Ile		
15	25	30	35
	Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa		
	40	45	50
	Xaa Asn Leu Asn Xaa Glu Asp Xaa Asp Ile Leu Xaa Glu		
	55	60	
20	Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa		
	65	70	75
	Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa		
	80	85	
	Ile Leu Xaa Asn Leu Xaa Pro Cys Xaa Pro Xaa Xaa Thr		
25	90	95	100
	Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly		
	105	110	115
	Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu		
	120	125	
30	Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln Thr Thr Leu		
	130		
	Ser Leu Ala Ile Phe [SEQ ID NO:7]		

wherein m is 0 or 1; Xaa at position 18 is Asn or Ile;
 35 Xaa at position 19 is Met, Ala or Ile; Xaa at position 20
 is Ile, Pro or Ile; Xaa at position 23 is Ile, Ala or
 Leu; Xaa at position 25 is Thr or His; Xaa at position 29
 is Gln, Arg, Val or Ile; Xaa at position 32 is Leu, Ala,

61

Asn or Arg; Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe, Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at position 45 is Gln, Val, or Met; Xaa at 5 position 46 is Asp or Ser; Xaa at position 49 is Met, Ile, Leu or Asp; Xaa at position 50 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at position 55 is Arg, Leu, or Thr; Xaa at position 56 is Pro or Ser; Xaa at position 59 is Glu or Leu; Xaa at position 60 is Ala or 10 Ser; Xaa at position 62 is Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, His or Gln; Xaa at position 69 is Gln or Glu; Xaa at position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at 15 position 79 is Lys, Arg or Ser; Xaa at position 82 is Leu, Glu, Val or Trp; Xaa at position 85 is Leu or Val; Xaa at position 87 is Leu, Ser, Tyr; Xaa at position 88 is Ala or Trp; Xaa at position 91 is Ala or Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or 20 Thr; Xaa at position 98 is His, Ile, or Thr; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at position 105 is Asn or Glu; Xaa at position 109 is Arg, Glu or Leu; Xaa at position 112 is Thr or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; 25 Xaa at position 117 is Thr or Ser; Xaa at position 120 is Asn, Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3.

30

10. The fusion protein of 9 wherein said human interleukin-3 mutant polypeptide is of the formula:

1	5	10
35 (Met _m -Alan) _p -Asn Cys Ser Xaa Xaa Xaa Asp Glu Xaa Ile		
	15	20
Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa		

	25	30	35
	Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa Ile Leu Xaa Glu		
	40	45	
5	Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa		
	50	55	60
	Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa		
	65	70	75
	Ile Leu Xaa Asn Xaa Xaa Pro Cys Xaa Pro Xaa Ala Thr		
10	80	85	
	Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly		
	90	95	100
	Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu		
	105	110	
15	Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln [SEQ ID NO:8]		

wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile; Xaa at position 6 is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xaa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Ile; Xaa at position 18 is Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile or Asp; Xaa at position 36 is Glu or Asp; Xaa at position 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala or Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is Val or Ser; Xaa at position 53 is Ser, Asn, His or Gln; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or

Trp; Xaa at position 71 is Leu or Val; Xaa at position 73 is Leu, Ser or Tyr; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87 is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95 is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His; Xaa at position 109 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125)human interleukin-3.

15

11. The fusion protein of 10 wherein said human interleukin-3 mutant polypeptide is of the Formula:

20

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro 25 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:9];

30

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro 35 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:10];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
5 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:11];

10

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu
15 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:12];

20

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
25 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:13];

30

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu
35 Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu

Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:14];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
5 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
10 Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:15];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
15 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
20 Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:16];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
25 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
30 His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:17];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
35 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln

Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
5 [SEQ ID NO:18];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
10 Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
15 [SEQ ID NO:19];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
20 Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
25 [SEQ ID NO:20];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn
Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg
30 Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
35 [SEQ ID NO:21];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
5 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:22];

10 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
15 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:23];

20 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro
25 Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile
His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu
Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
[SEQ ID NO:24];

30 Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His
Leu Lys Gln Pro Pro Leu Pro Leu Asp Phe Asn Asn Leu
Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg
Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu
Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
35 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

Gln [SEQ ID NO:25];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His
Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu
5 Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg
Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu
Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
10 Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:26];

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His
Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu
15 Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg
Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu
Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
20 Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
Gln [SEQ ID NO:27];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
25 Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu
Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro
Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
30 Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
Gln [SEQ ID NO:28];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
35 Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu

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Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro
Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
Gln [SEQ ID NO:29];

5

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
10 Glu Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu
Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro
Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
Gln [SEQ ID NO:30];

15

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
20 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:31];

25

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
30 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:32];

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu

Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:33];

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
15 Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:34];

20 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
25 Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:35];

30 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
35 Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
Gln [SEQ ID NO:36];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
5 Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
10 Gln [SEQ ID NO:37];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
15 Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
20 Gln [SEQ ID NO:38];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg
25 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Val
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
30 Gln [SEQ ID NO:39].

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg
35 Leu Ser Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:40]

- 5 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His
Leu Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
10 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:41]
- 15 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
20 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:42]
- 25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ala Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
30 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:43]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu

73

Asn Asp Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:44]

10 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
15 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:45]

20 Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro
Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
25 Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:46]

30

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
35 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro
Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys

Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:47] and

5

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His
Leu Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu
Asn Ser Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
10 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:48].

15

The following are examples of the fusion proteins of
the presents invention:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
20 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
25 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val
30 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
35 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Gln Pro Thr

Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:121]

5

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser

15

Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu

20

Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala

25

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg

30

Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:122]

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys

Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
5 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
10 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
15 [SEQ ID NO:123]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
20 Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
25 Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser
Gly Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
30 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
35 Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu

Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:124]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
5 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
10 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
15 Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
20 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln [SEQ ID NO:125]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
25 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
30 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
35 Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala

Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:126]

5 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
10 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
15 Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
20 Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:127]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
25 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
30 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
35 Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val

79

Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
5 Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
10 [SEQ ID NO:128]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
15 Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
20 Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
25 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
30 Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
35 [SEQ ID NO:129]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
5 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
10 Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
15 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
20 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:130]

25

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
30 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
35 Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
5 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
10 Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
15 Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
20 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:135]

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
30 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
35 Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu
Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met
Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe al Arg

Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
5 Gln Ala Gln Glu Gln Gln [SEQ ID NO:136]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
10 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
15 Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu
Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu
20 Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val
Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
25 Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:137]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
30 Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
35 Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala

Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
5 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
Glu Gln Ala Gln Glu Gln [SEQ ID NO:131]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
10 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
15 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
20 Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu
Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
25 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
Glu Gln Ala Gln Glu Gln [SEQ ID NO:132]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
30 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
35 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Ser Pro Gly Glu Pro Ser

Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu
Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
5 Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val
Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
10 Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:133]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
15 Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
20 Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
25 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
30 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
35 [SEQ ID NO:134]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
5 Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
10 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:138]

15 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
20 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val
Asn Ala Gly Gly Ser Gly Gly Ser Gly Gly Ser
25 Glu Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser Gly
Ser Glu Gly Gly Ser Gly Gly Ser Gly Ser Gly Asp
Phe Asp Tyr Glu Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
30 Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
35 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg

Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:139]

5 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
10 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Pro Ala Arg Ser Pro Ser Pro
15 Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala
Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met
Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln
Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln
Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr
20 Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro
Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe
Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp
Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:141]

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
30 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val
Asn Ala Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Ser
35 Glu Gly Gly Ser Gly Gly Ser Gly Ser Gly Ser Gly Ser Gly Asp
Phe Asp Tyr Glu Asn Met Ala Pro Ala Arg Ser Pro Ser Pro

Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu Ala
Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu Met
Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln
Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln
5 Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr
Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro
Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe
Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp
Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:142]
10
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
15 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Pro Val Asn Ala Gly Gly Ser Gly Gly Gly
20 Ser Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser Gly Gly
Ser Glu Gly Gly Ser Glu Gly Gly Ser Gly Gly Ser Gly Gly
Ser Gly Ser Gly Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Lys Leu Glu Gln Val
Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
25 Lys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
30 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
35 [SEQ ID NO:143]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
5 Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
10 Ser His Lys Ser Pro Asn Met Ala Pro Ala Arg Ser Pro Ser
Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala Ile Gln Glu
Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala Glu
Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu
Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys
15 Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu
Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr
Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser
Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe
Asp Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:144]
20
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
25 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
30 Gly Gly Ser Asn Met Ala Pro Val Pro Pro Gly Glu Asp
Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr Ser
Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly
Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met
Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn
35 Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly
Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu
Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe

Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr
Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu
Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu
Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met
5 Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln
Ser Ser Leu Arg Ala Leu Arg Gln Met [SEQ ID NO:145]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
10 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
15 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
20 Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Gly Ser Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro
25 Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
30 [SEQ ID NO:146]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
35 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu

Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
5 Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Gly Ser Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
10 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
15 Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
[SEQ ID NO:147]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
20 Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
25 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
30 Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Pro Gln Pro Pro
Val Asn Ala Gly Gly Ser Gly Gly Ser Gly Gly Gly
Ser Glu Gly Gly Ser Glu Gly Gly Ser Gly Gly Ser Gly Gly
Gly Ser Glu Gly Gly Ser Gly Gly Ser Gly Ser Gly Ser Gly
35 Asp Phe Asp Tyr Glu Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu
Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu

Met Asp Arg Asn Leu Arg Leu Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
5 Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln [SEQ ID NO:148]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
10 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
15 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
20 Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
25 Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
30 Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:149]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
35 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala

Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
5 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
10 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr
Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu
15 Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:150].

20 Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
25 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Ile Glu Gly Arg
Ile Ser Pro Gln Pro Pro Val Asn Ala Gly Gly Ser Gly
30 Gly Gly Ser Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser Gly
Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Gly Ser Gly
Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala
35

93

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro
Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn
5 Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:151]

10

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
15 Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Gly Ser
20 Gly Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser
Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
25 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
30 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:152]

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu

Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu
10 Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met
Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg
Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile
Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
15 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln [SEQ ID NO:153]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
20 Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
25 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Gly Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Thr Pro Leu Gly Pro Ala
30 Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln
Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
35 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp
Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp

Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe
Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
5 [SEQ ID NO:154]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu
Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
15 Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser
Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu
Ser His Lys Ser Pro Asn Met Ala Asn Cys Ser Ile Met Ile
Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu
Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu
20 Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val
Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
25 Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:155]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
30 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
35 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu

Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
5 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
10 Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:156]

15 Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
20 Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
25 Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met
30 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu
Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu
Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro
35 Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile
Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln

[SEQ ID NO:157]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly
5 Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
10 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu
Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
15 Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly
Gly Ser Pro Gly Gly Ser Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
20 Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
25 [SEQ ID NO:158]

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly
Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
30 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu His Ser Gly Leu
Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
35 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu

Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
Val Leu Arg His Leu Ala Gln Pro Tyr Val Glu Gly Gly Gly
Gly Ser Pro Gly Gly Ser Gly Gly Ser Asn Met Ala
Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
5 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn
Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys
Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile
10 Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:159]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
15 Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu
Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
20 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys
Asp Leu Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val
25 Leu His Ser Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu
Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu Gly
Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile
Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala
Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
30 Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr
Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His
Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly
Ser Thr Leu Cys Val Arg [SEQ ID NO:165].

35

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu

Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg
Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu
Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln
Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
5 Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys
Asp Leu Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val
10 Leu His Ser Arg Leu Ser Cys Pro Glu Val His Pro Leu
Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu Gly
Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile
Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala
Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
15 Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln
Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr
Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His
Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly
Ser Thr Leu Cys Val Arg [SEQ ID NO:166]

20 Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu
Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu
Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
25 Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr
Leu Leu Leu Glu Gly Val Met Ala Ala Arg Gln Gln Leu Gly
Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln
Val Arg Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro
30 Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys
Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val
Arg Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser
Gly Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp
Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu
35 Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met
Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile

100

Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln [SEQ ID NO:167]

5

Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu
Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu
Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu
Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln
10 Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr
Leu Leu Leu Glu Gly Val Met Ala Ala Arg Gln Gln Leu Gly
Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln
Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro
15 Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys
Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val
Arg Glu Phe His Ala Tyr Val Glu Gly Gly Gly Ser Pro
Gly Gly Ser Gly Gly Ser Asn Met Ala Asn Cys Ser
Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro
20 Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu
Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly
Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala
25 Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu
Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
[SEQ ID NO:168]

30 Materials and methods for fusion molecule Expression in
E. coli

Unless noted otherwise, all specialty chemicals are obtained from Sigma Co., (St. Louis, MO). Restriction endonucleases, T4 poly-nucleotides kinase, E. coli DNA polymerase I large fragment (Klenow) and T4 DNA ligase are obtained from New England Biolabs (Beverly, Massachusetts).

Escherichia coli strains

Strain JM101: delta (pro lac), supE, thi, F' (traD36, rpoAB, lacI-Q, lacZdeltaM15) (Messing, 1979). This strain can be obtained from the American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852, accession number 33876. MON105 (W3110 rpoH358) is a derivative of W3110 (Bachmann, 1972) and has been assigned ATCC accession number 55204. Strain GM48: dam-3, dcm-6, gal, ara, lac, thr, leu, tonA, tsx (Marinus, 1973) is used to make plasmid DNA that is not methylated at the sequence GATC.

Genes and plasmids

The gene used for hIL-3 production in *E. coli* is obtained from British Biotechnology Incorporated, Cambridge, England, catalogue number BBG14. This gene is carried on a pUC based plasmid designated pP0518. Many other human CSF genes can be obtained from R&D Systems, Inc. (Minn, MN) including IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, G-CSF, GM-CSF and LIF.

The plasmids used for production of hIL-3 in *E. coli* contain genetic elements whose use has been described (Olins et al., 1988; Olins and Rangwala, 1990). The replicon used is that of pBR327 (Covarrubias, et al., 1981) which is maintained at a copy number of about 100 in the cell (Soberon et al., 1980). A gene encoding the beta-lactamase protein is present on the plasmids. This protein confers ampicillin resistance on the cell. This resistance serves as a selectable phenotype for the presence of the plasmid in the cell.

For cytoplasmic expression vectors the transcription promoter is derived from the recA gene of *E. coli*. (Sancar et al., 1980). This promoter, designated precA, includes the RNA polymerase binding site and the lexA repressor binding site (the operator). This segment of DNA provides high level transcription that is regulated even when the recA promoter is on a plasmid with the pBR327 origin of replication (Olins et al., 1988) incorporated herein by reference.

The ribosome binding site used is that from gene 10 of phage T7 (Olins et al., 1988). This is encoded in a 100 base pair (bp) fragment placed adjacent to *preCA*. In the plasmids used herein, the recognition sequence for 5 the enzyme NcoI (CCATGG) follows the g10-L. It is at this NcoI site that the hIL-3 genes are joined to the plasmid. It is expected that the nucleotide sequence at this junction will be recognized in mRNA as a functional start site for translation (Olins et al., 1988). The 10 hIL-3 genes used were engineered to have a HindIII recognition site (AAGCTT) downstream from the coding sequence of the gene. At this HindIII site is a 514 base pair RsaI fragment containing the origin of replication of the single stranded phage f1 (Dente et al., 1983; 15 Olins, et al., 1990) both incorporated herein by reference. A plasmid containing these elements is pMON2341. Another plasmid containing these elements is pMON5847 which has been deposited at the American Type Culture Collection, 12301 Parklawn Drive, Rockville, 20 Maryland 20852 under the accession number ATCC 68912.

In secretion expression plasmids the transcription promoter is derived from the *ara B*, *A*, and *D* genes of *E. coli* (Greenfield et al., 1978). This promoter is designated pAraBAD and is contained on a 323 base pair 25 *SacII*, *BglII* restriction fragment. The *LamB* secretion leader (Wong et al., 1988, Clement et al., 1981) is fused to the N-terminus of the hIL-3 gene at the recognition sequence for the enzyme *NcoI* (5'CCATGG3'). The hIL-3 genes used were engineered to have a *HindIII* recognition 30 site (5'AAGCTT3') following the coding sequence of the gene.

Recombinant DNA methods

Synthetic gene assembly

The hIL-3 variant genes and other CSF genes can be 35 constructed by the assembly of synthetic oligonucleotides.

Synthetic oligonucleotides are designed so that they

would anneal in complementary pairs, with protruding single stranded ends, and when the pairs are properly assembled would result in a DNA sequence that encoded a portion of the desired gene. Amino acid substitutions in the hIL-3 gene are made by designing the oligonucleotides to encode the desired substitutions. The complementary oligonucleotides are annealed at concentration of 1 picomole per microliter in ligation buffer plus 50mM NaCl. The samples are heated in a 100 ml beaker of boiling water and permitted to cool slowly to room temperature. One picomole of each of the annealed pairs of oligonucleotides are ligated with approximately 0.2 picomoles of plasmid DNA, digested with the appropriate restriction enzymes, in ligation buffer (25 mM Tris pH 8.0, 10 mM MgCl₂, 10 mM dithiothreitol, 1 mM ATP, 2mM spermidine) with T4 DNA ligase obtained from New England Biolabs (Beverly, Massachusetts) in a total volume of 20 µl at room temperature overnight.

20 Polymerase Chain Reaction

Polymerase Chain Reaction (hereafter referred to as PCR) techniques (Saiki, 1985) used the reagent kit and thermal cycler from Perkin-Elmer Cetus (Norwalk, CT.). PCR is based on a thermostable DNA polymerase from Thermus aquaticus. The PCR technique is a DNA amplification method that mimics the natural DNA replication process in that the number of DNA molecules doubles after each cycle, in a way similar to *in vivo* replication. The DNA polymerase mediated extension is in a 5' to 3' direction. The term "primer" as used herein refers to an oligonucleotide sequence that provides an end to which the DNA polymerase can add nucleotides that are complementary to a nucleotide sequence. The latter nucleotide sequence is referred to as the "template", to which the primers are annealed. The amplified PCR product is defined as the region comprised between the 5' ends of the extension primers. Since the primers have defined

sequences, the product will have discrete ends, corresponding to the primer sequences. The primer extension reaction is carried out using 20 picomoles (pmoles) of each of the oligonucleotides and 1 picogram 5 of template plasmid DNA for 35 cycles (1 cycle is defined as 94 degrees C for one minute, 50 degrees C for two minutes and 72 degrees for three minutes.). The reaction mixture is extracted with an equal volume of phenol/chloroform (50% phenol and 50% chloroform, volume 10 to volume) to remove proteins. The aqueous phase, containing the amplified DNA, and solvent phase are separated by centrifugation for 5 minutes in a microcentrifuge (Model 5414 Eppendorf Inc, Fremont CA.). To precipitate the amplified DNA the aqueous phase is 15 removed and transferred to a fresh tube to which is added 1/10 volume of 3M NaOAc (pH 5.2) and 2.5 volumes of ethanol (100% stored at minus 20 degrees C). The solution is mixed and placed on dry ice for 20 minutes. The DNA is pelleted by centrifugation for 10 minutes in a 20 microcentrifuge and the solution is removed from the pellet. The DNA pellet is washed with 70% ethanol, ethanol removed and dried in a speedvac concentrator (Savant, Farmingdale, New York). The pellet is resuspended in 25 microliters of TE (20mM Tris-HCl pH 25 7.9, 1mM EDTA). Alternatively the DNA is precipitated by adding equal volume of 4M NH₄OAc and one volume of isopropanol [Treco et al., (1988)]. The solution is mixed and incubated at room temperature for 10 minutes and centrifuged. These conditions selectively precipitate DNA 30 fragments larger than ~ 20 bases and are used to remove oligonucleotide primers. One quarter of the reaction is digested with restriction enzymes [Higuchi, (1989)] and on completion heated to 70 degrees C to inactivate the enzymes.

35

Recovery of recombinant plasmids from ligation mixes

E. coli JM101 cells are made competent to take up

DNA. Typically, 20 to 100 ml of cells are grown in LB medium to a density of approximately 150 Klett units and then collected by centrifugation. The cells are resuspended in one half culture volume of 50 mM CaCl₂ and held at 4°C for one hour. The cells are again collected by centrifugation and resuspended in one tenth culture volume of 50 mM CaCl₂. DNA is added to a 150 microliter volume of these cells, and the samples are held at 4°C for 30 minutes. The samples are shifted to 42°C for one minute, one milliliter of LB is added, and the samples are shaken at 37°C for one hour. Cells from these samples are spread on plates containing ampicillin to select for transformants. The plates are incubated overnight at 37°C. Single colonies are picked, grown in LB supplemented with ampicillin overnight at 37°C with shaking. From these cultures DNA is isolated for restriction analysis.

Culture medium

LB medium (Maniatis et al., 1982) is used for growth of cells for DNA isolation. M9 minimal medium supplemented with 1.0% casamino acids, acid hydrolyzed casein, Difco (Detroit, Michigan) is used for cultures in which recombinant fusion molecule is produced. The ingredients in the M9 medium are as follows: 3g/liter KH₂PO₄, 6g/l Na₂HPO₄, 0.5 g/l NaCl, 1 g/l NH₄Cl, 1.2 mM MgSO₄, 0.025 mM CaCl₂, 0.2% glucose (0.2% glycerol with the AraBAD promoter), 1% casamino acids, 0.1 ml/l trace minerals (per liter 108 g FeCl₃·6H₂O, 4.0 g ZnSO₄·7H₂O, 7.0 CoCl₂·2H₂O, 7.0 g Na₂MoO₄·2H₂O, 8.0 g CuSO₄·5H₂O, 2.0 g H₃BO₃, 5.0 g MnSO₄·H₂O, 100 ml concentrated HCl). Bacto agar is used for solid media and ampicillin is added to both liquid and solid LB media at 200 micrograms per milliliter.

Production of fusion molecules in E. coli with vectors employing the recA promoter

E. coli strains harboring the plasmids of interest are grown at 37°C in M9 plus casamino acids medium with

shaking in a Gyrotory water bath Model G76 from New Brunswick Scientific (Edison, New Jersey). Growth is monitored with a Klett Summerson meter (green 54 filter), Klett Mfg. Co. (New York, New York). At a Klett value of 5 approximately 150, an aliquot of the culture (usually one milliliter) is removed for protein analysis. To the remaining culture, nalidixic acid (10mg/ml) in 0.1 N NaOH is added to a final concentration of 50 µg/ml. The cultures are shaken at 37°C for three to four hours after 10 addition of nalidixic acid. A high degree of aeration is maintained throughout the bacterial growth in order to achieve maximal production of the desired gene product. 15 The cells are examined under a light microscope for the presence of inclusion bodies. One milliliter aliquots of the culture are removed for analysis of protein content.

Fractionation of E. coli cells producing fusion proteins in the cytoplasm

The first step in purification of the fusion molecules is to sonicate the cells. Aliquots of the 20 culture are resuspended from cell pellets in sonication buffer: 10 mM Tris, pH 8.0, 1 mM EDTA, 50 mM NaCl and 0.1 mM PMSF. These resuspended cells are subjected to several repeated sonication bursts using the microtip from a Sonicator cell disrupter, Model W-375 obtained 25 from Heat Systems-Ultrasonics Inc. (Farmingdale, New York). The extent of sonication is monitored by examining the homogenates under a light microscope. When nearly all of the cells are broken, the homogenates are fractionated by centrifugation. The pellets, which 30 contain most of the inclusion bodies, are highly enriched for fusion proteins.

Methods: Extraction, Refolding and Purification of Fusion Molecules Expressed as Inclusion Bodies in E. coli.

These fusion proteins can be purified by a variety of standard methods. Some of these methods are described in detail in Methods in Enzymology, Volume 182 'Guide to Protein Purification' edited by Murray Deutscher, Academic Press, San Diego, CA (1990).

Fusion proteins which are produced as insoluble inclusion bodies in E. coli can be solubilized in high concentrations of denaturant, such as Guanidine HCl or Urea including dithiothreitol or beta mercaptoethanol as a reducing agent. Folding of the protein to an active conformation may be accomplished via sequential dialysis to lower concentrations of denaturant without reducing agent.

In some cases the folded proteins can be affinity purified using affinity reagents such as mabs or receptor subunits attached to a suitable matrix. Alternatively, (or in addition) purification can be accomplished using any of a variety of chromatographic methods such as: ion exchange, gel filtration or hydrophobic chromatography or reversed phase HPLC.

HIL-3 SANDWICH ELISA

The fusion protein concentrations can be determined using a sandwich ELISA based on an appropriate affinity purified antibody. Microtiter plates (Dynatech Immulon II) are coated with 150 µl goat-anti-rHIL-3 at a concentration of approximately 1 µg/ml in 100 mM NaHCO₃, pH 8.2. Plates are incubated overnight at room temperature in a chamber maintaining 100% humidity. Wells are emptied and the remaining reactive sites on the plate are blocked with 200 µl of solution containing 10 mM PBS, 3% BSA and 0.05% Tween 20, pH 7.4 for 1 hour at 37° C and 100% humidity. Wells are emptied and washed 4X with 150 mM NaCl containing 0.05% Tween 20 (wash buffer).

Each well then receives 150 μ l of dilution buffer (10 mM PBS containing 0.1% BSA, 0.01% Tween 20, pH 7.4), containing rhIL-3 standard, control, sample or dilution buffer alone. A standard curve is prepared with 5 concentrations ranging from 0.125 ng/ml to 5 ng/ml using a stock solution of rhIL-3 (concentration determined by amino acid composition analysis). Plates are incubated 2.5 hours at 37° C and 100% humidity. Wells are emptied and each plate is washed 4X with wash buffer. Each well 10 then received 150 μ l of an optimal dilution (as determined in a checkerboard assay format) of goat anti-rhIL-3 conjugated to horseradish peroxidase. Plates are incubated 1.5 hours at 37° C and 100% humidity. Wells are emptied and each plate is washed 4X with wash buffer. 15 Each well then received 150 μ l of ABTS substrate solution (Kirkegaard and Perry). Plates are incubated at room temperature until the color of the standard wells containing 5 ng/ml rhIL-3 had developed enough to yield an absorbance between 0.5-1.0 when read at a test 20 wavelength of 410 nm and a reference wavelength of 570 nm on a Dynatech microtiter plate reader. Concentrations of immunoreactive rhIL-3 in unknown samples are calculated from the standard curve using software supplied with the plate reader.

25 The following examples will illustrate the invention in greater detail although it will be understood that the invention is not limited to these specific examples.

EXAMPLE 1

30

Construction of expression plasmid for fusion molecules

Construction of a plasmid encoding a fusion protein composed of the IL-3 variant protein found in the plasmid, pMON13288 (United States Patent Application 35 Serial number PCT/US93/11197), followed by a factor Xa proteolytic cleavage site, followed by murine IgG 2b hinge region, in which the cysteines have replaced with

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serines, as the polypeptide linker sequence between the two proteins of the fusion and followed by G-CSF. The plasmid, pMON13288, is digested with EcoRI (which is internal in the IL-3 variant gene) and HindIII (which is after the stop codons for the IL-3 variant) and the 3900 base pair EcoRI, HindIII restriction fragment is purified. The genetic elements derived from pMON13288 are the beta-lactamase gene (AMP), pBR327 origin of replication, recA promoter, g10L ribosome binding site, the bases encoding amino acids 15-105 of (15-125)IL-3 variant gene, and phage f1 origin of replication. Pairs of complementary synthetic oligonucleotides are designed to replace the portion of the IL-3 variant gene after the EcoRI site (bases encoding amino acids 106-125), DNA sequence encoding the factor Xa cleavage site, DNA sequence encoding the polypeptide linker and AflIII restriction site to allow for cloning of the second gene in the fusion. When properly assembled the oligonucleotides result in a DNA sequence, encoding the above mentioned components in-frame, with EcoRI and HindIII restriction ends. Within this DNA sequence unique restriction sites are also created to allow for the subsequent replacement of specific regions with a sequence that has similar function (e.g... alternative polypeptide linker region). A unique SnaBI restriction site is created at the end of the 13288 gene which allows for the cloning of other genes in the C-terminus position of the fusion. A unique XmaI site is created between sequence encoding the factor Xa cleavage site and the region encoding the polypeptide linker. A unique AflIII site is created after the linker region that allows for the cloning of the N-terminal protein of the fusion. The 3900 base pair fragment from pMON13288 is ligated with the assembled oligonucleotides and transformed into an appropriate E. coli strain. The resulting clones are screened by restriction analysis and DNA sequenced to confirm that the desired DNA sequence are created. The resulting plasmid is used as an

intermediate into which other genes can be cloned as a NcoI, HindIII fragment into the AflIII and HindIII sites to create the desired fusion. The overhangs created by NcoI and AflIII are compatible but the flanking sequence of the restriction recognition sites are different. The NcoI and AflIII sites are lost as a result of the cloning. The above mentioned restriction sites are used as examples and are not limited to those described. Other unique restriction site may also be engineered which serve the function of allowing the regions to be replaced. The plasmid encoding the resulting fusion is DNA sequenced to confirm that the desired DNA sequence is obtained. Other IL-3 variant genes or other colony stimulating factor genes can be altered in a similar manner by genetic engineering techniques to create the appropriate restriction sites which would allow for cloning either into the C-terminal or N-terminal position of the fusion construct described above. Likewise alternative peptidase cleavage sites or polypeptide linkers can be engineered into the fusion plasmids.

EXAMPLE 2

Expression, Extraction, Refolding and Purification of Fusion Proteins, such as pMON13061, Expressed as Inclusion Bodies in E. coli

E. coli strains harboring the plasmids of interest are grown overnight at 37°C and diluted the following morning, approximately 1/50, in fresh M9 plus casamino acids medium. The culture is grown at 37°C for three to four hours to mid-log. (OD₆₀₀=~1) with vigorous shaking. Nalidixic acid (10mg/ml) in 0.1 N NaOH is added to a final concentration of 50 µg/ml. The cultures are grown at 37°C for three to four hours after the addition of nalidixic acid. A high degree of aeration is maintained throughout the bacterial growth in order to achieve maximal production of the desired fusion protein. In

cases where the fusion proteins are produced as insoluble inclusion bodies in E. coli the cells are examined under a light microscope for the presence of inclusion bodies.

E. coli cells containing fusion molecules in inclusion bodies were lysed by sonication. A 10% (w/v) suspension of the cells in 10 mM Tris-HCl pH 8.0 and 1 mM EDTA was subjected to three or four one minute bursts using a Sonicator cell disrupter, Model W-375, obtained from Heat Systems-Ultrasonics Inc. (Farmingdale, New York). The extent of cell disruption was monitored by examining the cells under a light microscope. When essentially all of the cells had been lysed, the inclusion bodies were harvested by centrifugation at 2800 x g for 20 min. The inclusion bodies were washed twice by suspending the inclusion body pellets to 10% in sonication buffer and centrifuging as above.

The fusion molecules were dissolved at one gram of inclusion bodies in 10 ml of 8 M urea with 50 mM Tris-HCl pH 9.5 and 5 mM DTT by blending with a Bio Homogenizer for 10 - 30 seconds and then gently stirring at 4°C for 1 - 2 hours. The dissolved fusion protein was clarified by centrifugation at 47,000 x g for 15 minutes.

Folding of the protein into an active conformation was done by diluting 8 fold with 2.3 M urea in 10 mM Tris-HCl pH 9.5 over 30 minutes to lower the concentration to 3 M urea. Folding of the fusion molecule was normally done between 2 and 3 M urea although higher concentrations of urea will also permit folding. The fusion was gently stirred under these conditions exposed to air until protein folding and formation of disulfide bonds was complete. The folding progress was monitored by reversed phase high performance liquid chromatography (RP - HPLC) using a 0.46 x 15 cm Vydac C 4 column (Hesperia, California) with a linear 35% to 65% acetonitrile (CH₃CN) / 0.1% trifluoroacetic acid (TFA) gradient over 25 minutes at 1 ml/minute.

After folding was complete, the pH of the fusion protein solution was lowered to 5.0 with glacial acetic acid and incubated at 4°C. After one hour, the solution was clarified by centrifugation at 47,000 x g for 15 minutes. The pH of the supernatant was lowered to 4.0 with acetic acid and clarified by filtration using a 0.45μ filter. The filtrate was dialyzed versus two, 100-fold, changes of 10 mM ammonium acetate pH 4.0. The pH of the dialyzed solution was increased to 6.5 with NaOH.

10 The neutralized solution was then loaded at 2 mg of fusion protein per 1 ml of resin on a DEAE Fast Flow column (Pharmacia Piscataway, NJ) equilibrated with 10 mM Tris-Cl pH 6.5. The fusion protein was eluted using a linear gradient from 50 to 150 mM NaCl in equilibration

15 buffer with a linear flow of 0.28 cm/min. for 12 hours. Using RP-HPLC analysis, fractions with a purity of 93% or better were pooled. The pooled fractions were dialyzed versus two, 100-fold, changes of 10 mM Tris-Cl pH 7.5. The dialyzed protein solution was sterile filtered, using

20 a 0.45μ filter, and stored at 4°C. RP-HPLC and cation exchange chromatography such as CM Fast Flow can also be used separately or in combination with DEAE chromatography to purify the fusion proteins.

The purified fusion protein was analyzed by RP-HPLC, electrospray mass spectrometry, IEF, and SDS-PAGE. The protein quantitation was done by amino acid composition and Bradford protein determination.

In some cases the folded proteins can be affinity purified using affinity reagents such as mAbs or receptor subunits attached to a suitable matrix. Alternatively, (or in addition) purification can be accomplished using any of a variety of chromatographic methods such as: ion exchange, gel filtration or hydrophobic chromatography or reversed phase HPLC.

35 These and other protein purification methods are described in detail in Methods in Enzymology, Volume 182 'Guide to Protein Purification' edited by Murray

Deutscher, Academic Press, San Diego, CA (1990).

EXAMPLE 3

Determination of the in vitro activity of fusion proteins

The protein concentration of the fusion protein can be determined using a sandwich ELISA based on an affinity purified polyclonal antibody. Alternatively the protein concentration can be determined by amino acid composition. The bioactivity of the fusion molecule can be determined in a number of in vitro assays compared with native IL-3, the IL-3 variant or G-CSF alone or together. One such assay is the AML-193 cell proliferation assay. AML-193 cells respond to IL-3 and G-CSF which allows for the combined bioactivity of the IL-3 variant/G-CSF fusion to be determined. In addition other factor dependent cell lines, such as M-NFS-60 (ATCC. CRL 1838) or 32D which are murine IL-3 dependent cell line, may be used. The activity of IL-3 is species specific whereas G-CSF is not, therefore the bioactivity of the G-CSF component of the IL-3 variant/G-CSF fusion can be determined independently. The methylcellulose assay can be used to determine the effect of the IL-3 variant/G-CSF fusion protein on the expansion of the hematopoietic progenitor cells and the pattern of the different types of hematopoietic colonies in vitro. The methylcellulose assay can provide an estimate of precursor frequency since one measures the frequency of progenitors per 100,000 input cells. Long term, stromal dependent cultures have been used to delineate primitive hematopoietic progenitors and stem cells. This assay can be used to determine whether the fusion molecule stimulates the expansion of very primitive progenitors and/or stem cells. In addition, limiting dilution cultures can be performed which will indicate the frequency of primitive progenitors stimulated by the fusion molecule.

The factor Xa cleavage site is useful to cleave the fusion protein after it is purified and re-folded to separate the IL-3 and G-CSF components of the fusion. After cleavage with factor Xa the IL-3 and G-CSF 5 components of the fusion can be purified to homogeneity and assayed separately to demonstrate that both components are in an active conformation after being expressed, refolded and purified as a fusion.

10

EXAMPLE 4Construction of pMON13018

Construction of pMON13018, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 3900 base pair 15 EcoRI, HindIII restriction fragment from pMON13288 was ligated with the following pairs of annealed complementary oligonucleotides:

Oligo #88Cterm1 [SEQ ID NO:91]
20 Oligo #88Cterm4 [SEQ ID NO:92]

Oligo #88Xa2 [SEQ ID NO:93]
Oligo #88Xa5 [SEQ ID NO:94]

25 Oligo #Glyn3 [SEQ ID NO:95]
Oligo #Glyn6 [SEQ ID NO:96]

The assembled oligonucleotides create EcoRI and HindIII restriction ends and the DNA sequence that encodes amino acids 106-125 of (15-125)hIL-3 variant 13288 and the polypeptide Linker 1 (Table 1) which is comprised of the factor Xa cleavage site and the amino acid sequence (Gly₃Ser)₂. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA 35 was sequenced to determine that the sequence was that of

the oligonucleotides. A schematic diagram of the construction of the plasmid, pMON13018, is shown in Figure 2.

5

EXAMPLE 5Construction of pMON13019

Construction of pMON13019, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 4014 base pair XmaI/AfIII restriction fragment from pMON13018 was ligated with the following pair of annealed complementary oligonucleotides:

- 15 Oligo #IgG2b1 [SEQ ID NO:97]
15 Oligo #IgG2b2 [SEQ ID NO:98]

The assembled oligonucleotides create XmaI and AfIII restriction ends and the DNA sequence that encodes amino acids 9-33 of the polypeptide Linker 4 (Table 1) which is comprised of the factor Xa cleavage site and the murine IgG2b hinge region. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. 25 The DNA was sequenced to determine that the sequence was that of the oligonucleotides.

EXAMPLE 6Construction of pMON13024

30 Construction of pMON13024, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 4091 base pair NheI,HindIII restriction fragment from pMON13010 was ligated with the following pair of annealed complementary
35 oligonucleotides:

- Oligo #GCSFSna1 [SEQ ID NO:99]

Oligo #GCSFSna2 [SEQ ID NO:100]

The assembled oligonucleotides create NheI and HindIII restriction ends, create a SnaBI restriction site at the 5' 3' end of the G-CSF gene, and the DNA sequence that encodes amino acids 155-175 of G-CSF. The stop codon after the G-CSF gene is eliminated and the DNA sequence of the SnaBI recognition site encodes amino acids Tyr Val in-frame at the C-terminus of G-CSF. The ligation 10 reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the oligonucleotides.

15

EXAMPLE 7**Construction of pMON13027**

Construction of pMON13027, an intermediate plasmid used for constructing plasmids containing DNA sequences 20 encoding fusion proteins. Plasmid, pMON13018, DNA was digested with restriction enzymes NcoI and SnaBI, resulting in a 3704 base pair NcoI, SnaBI fragment. Plasmid, pMON13024, DNA was digested with NcoI and SnaBI resulting in a 528 base pair NcoI, SnaBI fragment. The 25 restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to 30 confirm the correct insert.

EXAMPLE 8**Construction of pMON13032**

Construction of pMON13032, an intermediate plasmid used 35 for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON15930, DNA was digested with restriction enzymes NcoI and SnaBI,

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resulting in a 3829 base pair NcoI, SnaBI fragment. Plasmid, pMON13024, DNA was digested with NcoI and SnaBI, resulting in a 528 base pair NcoI, SnaBI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

10

EXAMPLE 9Construction of pMON13041

Construction of pMON13041, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The 4018 base pair SnaBI/XmaI restriction fragment from pMON13018 was ligated with the following pair of annealed complementary oligonucleotides:

20 Oligo #Lysxa1 [SEQ ID NO:101]
Oligo #Lysxa2 [SEQ ID NO:102]

The assembled oligonucleotides create SnaBI and XmaI restriction ends and the DNA sequence that encodes amino acids 1-8 of the polypeptide Linker 2 (Table 1) which is comprised of the factor Xa cleavage site in which the Arg is changed to Lys and the amino acid sequence (Gly₃Ser)₂. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the oligonucleotides.

35

EXAMPLE 10Construction of pMON13042

Construction of pMON13042, an intermediate plasmid used

for constructing plasmids containing DNA sequences encoding fusion proteins. The 4018 base pair SnaBI/XmaI restriction fragment from pMON13018 was ligated with the following pair of annealed complementary
5 oligonucleotides:

Oligo #Glyxa1 [SEQ ID NO:103]

Oligo #Glyxa2 [SEQ ID NO:104]

- 10 The assembled oligonucleotides create SnaBI and XmaI restriction ends and the DNA sequence that encodes the polypeptide Linker 3 (Table 1). Polypeptide Linker 3 is comprised of the following amino acid sequence Tyr Val Glu Gly Gly Gly Ser Pro (Gly₃Ser)₂ Asn [SEQ ID
15 NO:190]. The ligation reaction was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated from a colony grown in LB broth. The DNA was sequenced to determine that the sequence was that of the
20 oligonucleotides.

EXAMPLE 11

Construction of pMON13046

- Construction of pMON13046, an intermediate plasmid used
25 for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13018, DNA was digested with restriction enzymes NcoI and NsiI, resulting in a 3873 base pair NcoI,NsiI fragment.
Plasmid, pMON13416 (United States Patent Application
30 Serial number PCT/US93/11197) DNA, which encodes a hIL-3 variant, was digested with NcoI and NsiI, resulting in a 170 base pair NcoI, NsiI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101.
35 Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the

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correct insert.

EXAMPLE 12

- Construction of pMON13047
- 5 Construction of pMON13047, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13019, DNA was digested with restriction enzymes NcoI and NsiI, resulting in a 3918 base pair NcoI, NsiI fragment.
- 10 Plasmid, pMON13416, DNA was digested with NcoI and NsiI, resulting in a 170 base pair NcoI, NsiI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on
- 15 ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 13

- 20 Construction of pMON13478
- A pUC18 based plasmid containing the engineered gene encoding human granulocyte colony stimulating factor (hG-CSF) was obtained from R&D Systems (catalog # BBG13, Minneapolis MN). This plasmid was designated pMON13457.
- 25 The 3157 base pair ApaI, HindIII fragment from pMON13457 was ligated with the following pair of annealed complementary oligonucleotides:

- 28 Oligo #hgcsfma1 [SEQ ID NO:111]
30 Oligo #hgcsfma2 [SEQ ID NO:112]

- The assembled oligonucleotides create HindIII and ApaI restriction ends, an internal NcoI restriction site, the DNA sequence that encodes the first four amino acids of hG-CSF (Thr Pro Leu Gly) preceded by an initiator methionine followed by an alanine. The methionine and alanine were added for expression in E. coli. The

120

ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert.

5 The resulting plasmid was designated pMON13478.

EXAMPLE 14

Construction of pMON13498

The 3163 base pair NcoI,ApaI fragment from pMON13478 was
10 ligated with the following pair of annealed complementary
oligonucleotides:

Oligo #hgcsfat3 [SEQ ID NO:115]

Oligo #hgcsfat4 [SEQ ID NO:116]

15 The assembled oligonucleotides create NcoI and ApaI restriction ends, and maximizes A/T content of the DNA sequence that encodes the first four amino acids of mature hG-CSF (Thr Pro Leu Gly). The A/T content of the
20 DNA sequence was changed to increase protein expression levels in E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the
25 correct insert. The ApaI restriction end of the oligonucleotides is compatible with the ApaI site but ApaI recognition sequence is altered. The resulting plasmid was designated pMON13498. The foregoing modifications to the hG-CSF gene are found in the DNA
30 sequence [SEQ ID NO:178].

EXAMPLE 15

Construction of pMON13010

Plasmid, pMON5743 (Olins and Rangwala [1990]), DNA was
35 digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI,EcoRI fragment.
Plasmid, pMON13498, DNA was digested with NcoI and EcoRI,

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resulting in a 542 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13010, encodes the following amino acid sequence:

10 Peptide #

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe
Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
15 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp
20 Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly
Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
25 Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
30 Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala
Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val
Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro [SEQ ID NO:161]
35

DNA sequence # [SEQ ID NO:178] codes for the foregoing pMON13010 polypeptide.

EXAMPLE 16

40 Construction of pMON13499

The 3163 base pair NcoI, ApaI fragment from pMON13478 was ligated with the following pair of annealed complementary oligonucleotides:

45 Oligo #hgcsfat1 [SEQ ID NO:113]
Oligo #hgcsfat2 [SEQ ID NO:114]

The assembled oligonucleotides create NcoI and ApaI restriction ends, and maximizes A/T content of the DNA sequence that encodes the first three amino acids of hG-CSF (Thr Pro Leu). The A/T content of the DNA sequence was changed to increase expression levels in E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13499. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:177].

15

EXAMPLE 17Construction of pMON13033

The 3117 base pair ApaI,BstXI fragment from pMON13499 was ligated with the following pair of annealed complementary oligonucleotides:

20

Oligo #gcys18 [SEQ ID NO:107]

Oligo #gcys1810 [SEQ ID NO:108]

The assembled oligonucleotides create ApaI and BstXI restriction ends, and encodes amino acids 5 to 26 of hG-CSF except for amino acid 17 where the cysteine was replaced with serine. The cysteine was replaced with a serine to increase the in vitro refold efficiencies of the protein isolated from E. coli. The ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13033. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:179].

EXAMPLE 18Construction of pMON13037

Plasmid, pMON5743, DNA was digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI, EcoRI fragment. Plasmid, pMON13033, DNA was digested with NccI and EcoRI, resulting in a 542 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform E. coli K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13037, encodes the following amino acid sequence:

15 Peptide

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe
20 Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
25 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp
Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly
Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
30 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
35 Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala
Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val
40 Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
[SEQ ID NO:162]

45 DNA sequence # [SEQ ID NO:179] codes for the foregoing pMON13037 polypeptide.

EXAMPLE 19Construction of pMON13011

A pUC18 based plasmid containing the engineered gene encoding human granulocyte macrophage colony stimulating factor (hGM-CSF) was obtained from R&D Systems (catalog # BBG12, Minneapolis MN). This plasmid was designated pMON13458. The 2986 base pair NcoI,BsmI fragment from pMON13458 was ligated with the following pair of annealed complementary oligonucleotides:

10

Oligo #gm-aup [SEQ ID NO:105]

Oligo #gm-alow [SEQ ID NO:106]

The assembled oligonucleotides create NcoI and BsmI restriction ends and the DNA sequence that encodes the first nineteen amino acids of hGM-CSF. The DNA sequence encoding amino acids 3, 4, 5, 7, 9, 11, 12, 13 and 15 were changed to *E.coli* preferred codons to increase expression levels in *E. coli*. The ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13011. The foregoing modifications to the hGM-CSF gene are found in the DNA sequence [SEQ ID NO:176].

EXAMPLE 20Construction of pMON13012

30 Plasmid, pMON5743, DNA was digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI,EcoRI fragment. Plasmid, pMON13011, DNA was digested with NcoI and EcoRI, resulting in a 398 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, 35 and the ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA

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was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13012, encodes the following amino acid sequence:

5 Peptide #

Met Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu
His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser
10 Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser
Glu Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu
15 Glu Leu Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys
Gly Pro Leu Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro
Pro Thr Pro Glu Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu
20 Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu Leu Val Ile Pro Phe
Asp Cys Trp Glu Pro Val Gln Glu [SEQ ID NO:160]

25

DNA sequence # [SEQ ID NO:176] codes for the foregoing pMON13012 polypeptide.

30

EXAMPLE 21

Construction of pMON5865

A pUC18 based plasmid containing the engineered gene encoding human interleukin-6 (hIL-6) was obtained from British Biotech (catalog # BBG17). The 3170 base pair HindIII/BstXI fragment from this plasmid was ligated with the following pair of annealed complementary oligonucleotides:

Oligo #HIL6231 [SEQ ID NO:109]

40 Oligo #HIL6232 [SEQ ID NO:110]

The assembled oligonucleotides create HindIII and BstXI restriction ends and the DNA sequence that encodes the first ten amino acids of hIL-6 plus Met Ala at the N-terminus for E. coli protein expression. The

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oligonucleotides also create an NcoI site at the 5' end of the gene. The codons encoding the first ten amino acids were changed to *E. coli* preferred to increase expression levels in *E. coli*. The ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated and sequenced to confirm the correct insert. The resulting plasmid was designated pMON5865. The foregoing modifications to the hG-CSF gene are found in the DNA sequence [SEQ ID NO:175].

EXAMPLE 22Construction of pMON13040

15 Plasmid pMON5743 DNA was digested with restriction enzymes NcoI and EcoRI, resulting in a 3633 base pair NcoI, EcoRI fragment. Plasmid, pMON5865, DNA was digested with NcoI and EcoRI, resulting in a 572 base pair NcoI, EcoRI fragment. The restriction fragments were ligated, 20 and the ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, 25 pMON13040, encodes the following amino acid sequence:

Peptide #

Met Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala
30 Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln
Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr
35 Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala
Glu Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys
Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile
40 Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn
Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser

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Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu
Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu
5 Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr
His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu
Arg Ala Leu Arg Gln Met [SEQ ID NO:163]

10

DNA sequence # [SEQ ID NO:175] codes for the foregoing pMON13040 polypeptide.

EXAMPLE 23

15 Construction of pMON15931

Construction of pMON15931, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The DNA sequence encoding the (Gly-Ser)-rich spacer region of the pIII protein of the 20 filamentous bacteriophage fd (Schaller et al., 1975) was amplified using PCR techniques. A plasmid containing the gene encoding the pIII protein of the filamentous bacteriophage fd served as the template for the PCR reaction using the following oligonucleotides as primers:

25

Oligo # **prefor** [SEQ ID NO:117]
Oligo # **revpre** [SEQ ID NO:118]

30 The PCR primer extension reaction generated the following DNA sequence:

CCTGTCAACC CGGGCGGC GG CTCTGGTG GT GGTTCTGGTG CGGGCTCTGA
GGGTGGCGGC TCTGAGGGTG GC GGTTCTGA GGGTGGCGGC TCTGAGGGTG
35 CGGGTTCCGG TGGCGGCTCC GGTCCGGTA ACATGTATTA TGA
[SEQ ID NO:181]

40 The foregoing DNA sequence encodes amino acids 9 - 49 of the polypeptide Linker 7 (Table 1) which is comprised of the factor Xa cleavage site and the (Gly-Ser)-rich region of the pIII protein of the fd bacteriophage. The

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- PCR generated fragment was digested with XmaI and AflIII and ligated with the 4014 base pair XmaI, AflIII fragment from pMON13018. The ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 2410 Construction of pMON15930

Construction of pMON15930, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. The DNA sequence encoding the (Gly-Ser)-rich spacer region with a few flanking amino acids of the pIII protein of the filamentous bacteriophage fd (Schaller et al., 1975) was amplified using PCR techniques. A plasmid containing the gene encoding the pIII protein of the filamentous bacteriophage fd served as the template for the PCR reaction using the following oligonucleotides as primers:

Oligo # **forxtra** [SEQ ID NO:119]

Oligo # **xtrarev** [SEQ ID NO:120]

- 25 The PCR primer extension reaction generated the following DNA sequence:

ATCGTCTGAC CTCCCGGGCC TCCTGTCAAT GCTGGCGGCG GCTCTGGTGG

30 TGGTTCTGGT GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG
AGGGTGGCGG CTCTGAGGGT GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT
GATTTGATT ATGAAAACAT GTCAAACGCT [SEQ ID NO:182]

- 35 The foregoing DNA sequence encodes amino acids 9 - 70 of the polypeptide Linker 8 (Table 1) which is comprised of the factor Xa cleavage site and the (Gly-Ser)-rich region of the pIII protein of the fd bacteriophage. The 40 PCR generated fragment was digested with XmaI and AflIII

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and ligated with the 4014 base pair XmaI,AfI_{III} fragment from pMON13018. The ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert.

EXAMPLE 25

Construction of pMON13038

10 Construction of pMON13038, an intermediate plasmid used for constructing plasmids containing DNA sequences encoding fusion proteins. Plasmid, pMON13019, DNA was digested with restriction enzymes NcoI and SnaBI, resulting in a 3749 base pair NcoI,SnaBI fragment.

15 Plasmid, pMON13024, DNA was digested with NcoI and SnaBI, resulting in a 528 base pair NcoI, SnaBI fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on

20 ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The resulting plasmid was designated pMON13038.

EXAMPLE 26

Construction of pMON13021

Plasmid, pMON13018, DNA was digested with restriction enzymes AfI_{III} and Hind_{III}, resulting in a 4023 base pair AfI_{III},Hind_{III} fragment. Plasmid, pMON13288, DNA was digested with NcoI and Hind_{III}, resulting in a 345 base pair NcoI, Hind_{III} fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates.

35 Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. A schematic diagram of the construction of the plasmid,

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pMON13021, is shown in Figure 2. The plasmid, pMON13021, encodes the fusion with the following amino acid sequence:

5 Peptide # [SEQ ID NO:125]

DNA sequence # [SEQ ID NO:54] codes for the foregoing pMON13021 polypeptide.

10 EXAMPLE 27

Construction of pMON13022

Plasmid, pMON13018, DNA was digested with restriction enzymes AflIII and HindIII, resulting in a 4023 base pair AflIII, HindIII fragment. Plasmid, pMON13012, DNA was 15 digested with NcoI and HindIII, resulting in a 586 base pair NcoI, HindIII fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform *E. coli* K-12 strain JM101. Transformant bacteria were selected on ampicillin-containing plates.
20 Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The plasmid, pMON13022, encodes the fusion with the following amino acid sequence:
25 Peptide # [SEQ ID NO:141]

DNA sequence # [SEQ ID NO:55] codes for the foregoing pMON13022 polypeptide.

30 EXAMPLE 28-62

Further examples of fusion proteins, comprised in part of hIL-3 variant(s) are shown in Table 2. The plasmids 35 containing the genes encoding the fusion proteins in Table 2 were constructed by methods described in Materials and Methods and in Examples contained herein, particularly Examples 1, 9, 10, 26 and 27. DNA restriction fragments, indicated in Table 2 were ligated

and the resulting E. coli expression plasmids (Table 2) contain DNA sequences which encode the indicated polypeptide fusions (Table 2). The polypeptide fusions are comprised of two colony stimulating factors (R₁ and R₂) fused through a polypeptide linker (L) (Table 1), represented by the formula, R₁-L-R₂. Some of the genes encoding the polypeptide fusions in Table 2 were transferred from the E. coli expression vector, as a NcoI,HindIII restriction fragment into a mammalian cell (BHK) expression vector pMON3934. The E. coli and BHK expression plasmids are shown in Table 2. The biological activity, growth promoting activity in AML193.1.3 cells, for some of the polypeptide fusions in Table 2 is shown in Table 3. The biological activity, as evaluated in the methylcellulose assay, for some of the fusions in Table 2 is shown in Figures 3-7.

20

Table 1.
Polypeptide linker nomenclature and amino acid sequence.

Polypeptide Linker Designation	Amino Acid Sequence
Linker 1	YVIEGRISP(GGGS) _{2N} [SEQ ID NO:188]
Linker 2	YVIEGKISP(GGGS) _{2N} [SEQ ID NO:189]
Linker 3	YVEGGGGSP(GGGS) _{2N} [SEQ ID NO:190]
Linker 4	YVIEGRISPGEPSGPPISTINPSPPSKESHKSPN [SEQ ID NO:191]
Linker 5	YVIEGKISPGEPSGPPISTINPSPPSKESHKSPN [SEQ ID NO:192]
Linker 6	YVEGGGGSPGEPSGPPISTINPSPPSKESHKSPN [SEQ ID NO:193]

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Linker 7	YVIEGRISP(GGGS) ₃ (EGGGS) ₄ GGGS ₂ SGSN [SEQ ID NO:194]
Linker 8	YVIEGRISPQPPVNA(GGGS) ₃ (EGGGS) ₄ GGGS ₂ SGDFDYEN [SEQ ID NO:195]
Linker 9	EFHAYVEGGGGSP(GGGS) ₂ N [SEQ ID NO:196]

Table 2

Example Number	vector fragment	insert fragment	E. coli PMON	BHK PMON	R1	Linker	R2	DNA ISEQ ID NO: 1	Polypeptide ISEQ ID NO: 1
?n	PMON13018 4023 bp AflII/HindIII	PMON13010 556 bp NcoI, HindIII	13021	3987	13288	Linker 1	G-CSF	[SEQ ID NO:51]	[SEQ ID NO:127]
26	PMON13018 4023 bp AflII/HindIII	PMON13288 345 bp NcoI, HindIII	13021	3988	13288	Linker 1	G-CSF	[SEQ ID NO:54]	[SEQ ID NO:125]
27	PMON13018 4023 bp AflII/HindIII	PMON13012 412 bp NcoI, HindIII	13022	1089	13288	Linker 1	GN-CSF	[SEQ ID NO:55]	[SEQ ID NO:141]
29	PMON13021 4029 bp NcoI,SnaBI	PMON13024 528 bp NcoI, SnaBI	13026	3995	13288	Linker 1	GN-CSF	[SEQ ID NO:56]	[SEQ ID NO:146]
10	PMON15931 4148 bp AflII/HindIII	PMON13037 556 bp NcoI, HindIII	13062	26412	13288	Linker 8	G-CSF Ser17	[SEQ ID NO:65]	[SEQ ID NO:149]
11	PMON15931 4148 bp AflII/HindIII	PMON13012 412 bp NcoI, HindIII	13031	3998	13288	Linker 8	GN-CSF	[SEQ ID NO:66]	[SEQ ID NO:147]
12	PMON15930 4119 bp AflII/HindIII	PMON13010 556 bp NcoI, HindIII	15037	26405	13288	Linker 7	G-CSF	[SEQ ID NO:67]	[SEQ ID NO:143]
14	PMON13019 4068 bp AflII/HindIII	PMON13010 556 bp NcoI, HindIII	13014	26406	13288	Linker 4	G-CSF	[SEQ ID NO:68]	[SEQ ID NO:120]
14	PMON13019 4068 bp AflII/HindIII	PMON13012 412 bp NcoI, HindIII	13015	26407	13288	Linker 4	GN-CSF	[SEQ ID NO:69]	[SEQ ID NO:144]
35	PMON13019 4068 bp AflII/HindIII	PMON13288 345 bp NcoI, HindIII	13036	26408	13288	Linker 4	G-CSF	[SEQ ID NO:62]	[SEQ ID NO:141]
16	PMON13010 4257 bp AflII/HindIII	PMON13288 345 bp NcoI, HindIII	13061	26433	13288	Linker 4	G-CSF	[SEQ ID NO:73]	[SEQ ID NO:150]
17	PMON13012 4337 bp AflII/HindIII	PMON13288 345 bp NcoI, HindIII	13064	26414	13288	Linker 8	G-CSF	[SEQ ID NO:74]	[SEQ ID NO:151]
18	PMON13018 4023 bp AflII/HindIII	PMON13037 556 bp NcoI, HindIII	13039	26415	13288	Linker 1	G-CSF Ser17	[SEQ ID NO:56]	[SEQ ID NO:122]
19	PMON13027 4212 bp AflII/HindIII	PMON13416 345 bp NcoI, HindIII	13043	26416	13288	Linker 1	G-CSF	[SEQ ID NO:75]	[SEQ ID NO:147]

Table 2 cont

Example Number	vector fragment	insert fragment	E. coli PMON	BHK PMON	R1	Linker	R2	DNA [SEQ ID NO:]	Polypeptide [SEQ ID NO:]
40	PMON13012 4337 bp AflII/HindIII	PMON13416 345 bp NcoI, HindIII	11044	26417	G-CSF	Linker 8	13416	[SEQ ID NO: 761]	[SEQ ID NO: 148]
41	PMON13018 4257 bp AflII/HindIII	PMON13416 345 bp NcoI, HindIII	11045	26418	G-CSF	Linker 4	13416	[SEQ ID NO: 771]	[SEQ ID NO: 149]
42	PMON13041 4023 bp AflII/HindIII	PMON13037 556 bp NcoI, HindIII	11054	26424	13288	Linker 2	G-CSF Ser17	[SEQ ID NO: 591]	[SEQ ID NO: 123]
43	PMON13042 4023 bp AflII/HindIII	PMON13037 556 bp NcoI, HindIII	11056	26426	13288	Linker 3	G-CSF Ser17	[SEQ ID NO: 601]	[SEQ ID NO: 124]
44	PMON13041 4023 bp AflII/HindIII	PMON13288 345 bp NcoI, HindIII	11055	26425	13288	Linker 2	13288	[SEQ ID NO: 581]	[SEQ ID NO: 126]
45	PMON13042 4023 bp AflII/HindIII	PMON13288 345 bp NcoI, HindIII	11057	26427	13288	Linker 3	13288	[SEQ ID NO: 611]	[SEQ ID NO: 127]
46	PMON13047 4068 bp AflII/HindIII	PMON13416 345 bp NcoI, HindIII	11052	26422	13416	Linker 4	13416	[SEQ ID NO: 821]	[SEQ ID NO: 137]
47	PMON13047 4068 bp AflII/HindIII	PMON13037 556 bp NcoI, HindIII	11053	26423	13416	Linker 4	G-CSF Ser17	[SEQ ID NO: 831]	[SEQ ID NO: 138]
48	PMON13023 4409 bp NsII, NcoI	PMON13416 170 bp NcoI, NsII	11066	26436	13416	Linker 1	G-CSF	[SEQ ID NO: 841]	[SEQ ID NO: 134]
49	PMON13046 4023 bp AflII/HindIII	PMON13037 556 bp NcoI, HindIII	11051	26421	13416	Linker 1	G-CSF Ser17	[SEQ ID NO: 851]	[SEQ ID NO: 135]
50	PMON13046 4023 bp AflII/HindIII	PMON13416 345 bp NcoI, HindIII	11050	26420	13416	Linker 1	13416	[SEQ ID NO: 861]	[SEQ ID NO: 146]
51	PMON13041 3994 bp XmaI, HindIII	PMON13034 630 bp XmaI, HindIII	11058	26428	13288	Linker 5	G-CSF	[SEQ ID NO: 701]	[SEQ ID NO: 129]
52	PMON13042 3994 bp XmaI, HindIII	PMON13034 630 bp XmaI, HindIII	11060	26430	13288	Linker 6	G-CSF	[SEQ ID NO: 711]	[SEQ ID NO: 130]
53	PMON13041 3994 bp XmaI, HindIII	PMON13036 419 bp XmaI, HindIII	11059	26429	13288	Linker 5	13288	[SEQ ID NO: 631]	[SEQ ID NO: 131]

Table 2 cont.

Example Number	vector fragment	Insert fragment	E. coli BHK DMON	R1	Linker	R2	DNA SEQ ID NO:	Polypeptide SEQ ID NO:
54	PMON13042 3994 bp XmaI, HindIII	PMON13016 419 bp XmaI, HindIII	13061 26431	13288 Linker 6	13288 Linker 6	13288 Linker 6	1 SEQ ID NO: 641	1 SEQ ID NO: 1331
55	PMON13018 4023 bp AflII, HindIII	PMON13040 586 bp NcoI, HindIII	13049 26435	13288 Linker 1	13288 Linker 1	13288 Linker 1	1 SEQ ID NO: 571	1 SEQ ID NO: 1451
56	PMON13056 4409 bp NcoI, NsiI	PMON13416 170 bp NcoI, NsiI	13145	13416 Linker 1	13416 Linker 1	13416 Linker 1	1 SEQ ID NO: 871	1 SEQ ID NO: 1571
57	PMON13053 4599 bp SnaBI, XmaI	GlyXal [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13146	13416 Linker 6	13416 Linker 6	13416 Linker 6	1 SEQ ID NO: 891	1 SEQ ID NO: 1541
58	PMON13050 4343 bp SnaBI, XmaI	GlyXal [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13147	13416 Linker 3	13416 Linker 3	13416 Linker 3	1 SEQ ID NO: 881	1 SEQ ID NO: 1531
59	PMON13052 4388 bp SnaBI, XmaI	GlyXal [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13148	13416 Linker 6	13416 Linker 6	13416 Linker 6	1 SEQ ID NO: 901	1 SEQ ID NO: 1571
60	PMON13043 4532 bp SnaBI, XmaI	GlyXal [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13151	13416 Linker 1	13416 Linker 1	13416 Linker 1	1 SEQ ID NO: 781	1 SEQ ID NO: 1581
61	PMON13151 4479 bp NcoI, BstXI	PMON13017 78 bp NcoI, BstXI	13149	13416 Linker 3	13416 Linker 3	13416 Linker 3	1 SEQ ID NO: 801	1 SEQ ID NO: 1591
62	PMON13045 4577 bp SnaBI, XmaI	GlyXal [SEQ ID NO: 103] GlyXa2 [SEQ ID NO: 104]	13152	13416 Linker 6	13416 Linker 6	13416 Linker 6	1 SEQ ID NO: 791	1 SEQ ID NO: 1561
63	PMON13152 4524 bp NcoI/BstXI	PMON13037 78 bp NcoI, BstXI	13150	13416 Linker 6	13416 Linker 6	13416 Linker 6	1 SEQ ID NO: 811	1 SEQ ID NO: 1571

Example 635 Isolation of 1-332 and 1-153 amino acid forms of c-mpl ligand (Mega-CSF)

A. Reverse transcriptase reaction (c-mpl ligand sequence based on Genbank accession #L33410). Human fetal liver, 10 A+ RNA was obtained from Clontech (Palo Alto, CA). The first strand cDNA reactions was carried out using a cDNA Cycle™ Kit obtained from Invitrogen (San Diego, CA).

B. Polymerase chain reactions

15 Following the reverse transcriptase (RT) reaction, the 1-332 c-mpl ligand was amplified by PCR using the oligonucleotide primers c-mplNcoI [SEQ ID NO:169], which created an NcoI site immediately preceding the 5' end of the gene and c-mplEcoRI [SEQ ID NO:170] which created an 20 EcoRI site immediately 3' to the stop codon. Following the RT reaction, the 1-153 c-mpl ligand was amplified using the c-mplNcoI [SEQ ID NO:169] primer and the 3' primer, c-mplHindIII [SEQ ID NO:171] which created a stop 25 codon and an HindIII site immediately 3' to the codon for amino acid 153.

Example 64Construction of pMON26448

30 The 1-153 c-mpl ligand PCR product was digested with NcoI and HindIII restriction enzymes for subcloning into pMON3934. pMON3934, a mammalian expression vector, is derived from pMON3359 [Hippenmeyer et al., (1993)], but it contains a modified human IL 3 signal peptide sequence 35 in addition to the IE110 promoter and poly-A signal. The signal peptide sequence is flanked by BamHI and NcoI restriction enzyme sites, which facilitates cloning and

expression of genes as NcoI, HindIII fragments. The HindIII site is 3' to the NcoI site. The DNA sequence of the signal peptide is shown below (restriction enzyme sites are indicated above). The ATG (methionine) codon within the NcoI site is in-frame with the initiator ATG of the signal peptide (underlined);

BamHI
GGATCCACCATGAGCCGCCTGCCCGTCCTGCTCCTGCTCCAACTCCTGGTCCGCCCC
MetSerArgLeuProValLeuLeuLeuGlnLeuLeuValArgPro
NcoI
GCCATGG [SEQ ID NO:140]
AlaMet [SEQ ID NO:187]

15

The resulting plasmid was designated pMON26448. The plasmid, pMON26448, encodes the fusion with the following amino acid sequence:

20 Peptide #
Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser
Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln
25 Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala
Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr
Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly
30 Val Met Ala Ala Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser
Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala
35 Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr
Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His
Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser
40 Thr Leu Cys Val Arg [SEQ ID NO:164]

45 DNA sequence # [SEQ ID NO:180] codes for the foregoing pMON26448 polypeptide.

EXAMPLE 65

Isolation of cDNA sequence amino acid 1-153 form of c-mpl ligand (Mega-CSF) with modified C-terminus

A. Reverse transcriptase reaction (c-mpl ligand sequence based on Genbank accession #L33410). Human fetal liver A+ RNA was obtained from Clontech (Palo Alto, CA). The 5 first strand cDNA reactions was carried out using a cDNA Cycle™ Kit obtained from Invitrogen (San Diego, CA).

B. Polymerase chain reactions

Following the reverse transcriptase (RT) reaction, the 1-
10 332 c-mpl ligand was amplified by PCR using the
oligonucleotide primers c-mplNcoI [SEQ ID NO:169], which
created an NcoI site immediately preceeding the 5' end of
the gene and c-mplEcoRI [SEQ ID NO:170] which created an
EcoRI site immediately 3' to the stop codon. Using the
15 above PCR reaction as the template, the 1-153 c-mpl
ligand was amplified using the c-mplNcoI [SEQ ID NO:169]
primer and the 3' primer, Eco-mpl [SEQ ID NO:172] which
created an EcoRI site immediately 3' to the codon for
amino acid 153 and encodes the amino acids Glu Phe in-
20 frame at the C-terminus of the gene. The 1-153 c-mpl
ligand PCR product was digested with NcoI and EcoRI. The
resulting 467 base pair NcoI,EcoRI restriction fragment
was subsequently cloned into intermediate plasmids,
described in the examples herein, to create fusion
25 polypeptides.

Example 65Construction of pMON26460

5 Plasmid, pMON13018, DNA was digested with restriction enzymes AflIII and HindIII, resulting in a 4023 base pair AflIII, HindIII fragment. Plasmid, pMON26448, DNA was digested with NcoI and HindIII, resulting in a 468 base pair NcoI, HindIII fragment. The restriction fragments were ligated, and the ligation reaction mixture was used to transform *E. coli*. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The *E. coli* expression plasmid, pMON26460, encodes the fusion with the following amino acid sequence:

Peptide # [SEQ ID NO:165]

20 DNA sequence # [SEQ ID NO:183] codes for the foregoing pMON26460 polypeptide. The gene encoding the fusion was transferred as a NcoI, HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated 25 pMON26463.

Example 67Construction of pMON26461

30 The 4029 base pair NcoI, SnaBI fragment from, pMON13057, was ligated with the 467 base pair NcoI, EcoRI PCR generated fragment from Example 65 and two oligonucleotides (Ecosna1 [SEQ ID NO:173], Ecosna2 [SEQ ID NO:174]) The ligation reaction mixture was used 35 to transform *E. coli*. Transformant bacteria were selected on ampicillin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and

140

sequenced to confirm the correct insert. The E. coli expression plasmid, pMON26461, encodes the fusion with the following amino acid sequence:

5 Peptide # [SEQ ID NO:168]

DNA sequence # [SEQ ID NO:186] codes for the foregoing pMON26461 polypeptide.

The gene encoding the fusion was transferred as a 10 NcoI,HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated pMON26464.

Example 68

15 Construction of pMON26471

The 3285 base pair NcoI,HindIII fragment from, pMON3935, was ligated with the 362 base pair NcoI,SmaI restriction fragment from pMON26426 and the 494 base pair SmaI,HindIII restriction fragment from pMON26460, and the 20 ligation reaction mixture was used to transform E. coli. Transformant bacteria were selected on spectinomycin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The E. coli expression plasmid, 25 pMON26471, encodes the fusion with the following amino acid sequence:

Peptide # [SEQ ID NO:166]

30 DNA sequence # [SEQ ID NO:184] codes for the foregoing pMON26471 polypeptide.

The gene encoding the fusion was transferred as a NcoI,HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated 35 pMON26473.

Example 69

Construction of pMON26472

The 3285 base pair NcoI,HindIII fragment from, pMON3935,

was ligated with the 481 base pair NcoI,SnaBI restriction fragment from pMON26461 and the 399 base pair SnaBI,HindIII restriction fragment from pMON3988, and the ligation reaction mixture was used to transform *E. coli*.
5 Transformant bacteria were selected on spectinomycin-containing plates. Plasmid DNA was isolated, analyzed by restriction analysis, and sequenced to confirm the correct insert. The *E. coli* expression plasmid, pMON26472, encodes the fusion with the following amino
10 acid sequence:

Peptide # [SEQ ID NO:167]

DNA sequence # [SEQ ID NO:185] codes for the
15 foregoing pMON26472 polypeptide.
The gene encoding the fusion was transferred as a NcoI,HindIII fragment to the mammalian expression vector, pMON3934, and the resulting plasmid was designated pMON26474.

20 Various other examples will be apparent to the person skilled in the art after reading the present disclosure without departing from the spirit and scope of the invention. It is intended that all such other examples be included within the scope of the appended
25 claims.

AML Proliferation Assay for Bioactive Human Interleukin-3

The factor-dependent cell line AML 193 was obtained from the American Type Culture Collection (ATCC, 30 Rockville, MD). This cell line, established from a patient with acute myelogenous leukemia, is a growth factor dependent cell line which displayed enhanced growth in GM-CSF supplemented medium (Lange, B., et al., (1987); Valtieri, M., et al., (1987)). The ability of AML 35 193 cells to proliferate in the presence of human IL-3 has also been documented. (Santoli, D., et al., (1987)). A cell line variant was used, AML 193 1.3, which was adapted for long term growth in IL-3 by washing out the

growth factors and starving the cytokine dependent AML 193 cells for growth factors for 24 hours. The cells are then replated at 1×10^5 cells/well in a 24 well plate in media containing 100 U/ml IL-3. It took approximately 2 months for the cells to grow rapidly in IL-3. These cells are maintained as AML 193 1.3 thereafter by supplementing tissue culture medium (see below) with human IL-3.

AML 193 1.3 cells are washed 6 times in cold Hanks balanced salt solution (HBSS, Gibco, Grand Island, NY) by centrifuging cell suspensions at $250 \times g$ for 10 minutes followed by decantation of the supernatant. Pelleted cells are resuspended in HBSS and the procedure is repeated until six wash cycles are completed. Cells washed six times by this procedure are resuspended in tissue culture medium at a density ranging from 2×10^5 to 5×10^5 viable cells/ml. This medium is prepared by supplementing Iscove's modified Dulbecco's Medium (IMDM, Hazelton, Lenexa, KS) with albumin, transferrin, lipids and 2-mercaptoethanol. Bovine albumin (Boehringer-Mannheim, Indianapolis, IN) is added at 500 $\mu\text{g}/\text{ml}$; human transferrin (Boehringer-Mannheim, Indianapolis, IN) is added at 100 $\mu\text{g}/\text{ml}$; soybean lipid (Boehringer-Mannheim, Indianapolis, IN) is added at 50 $\mu\text{g}/\text{ml}$; and 2-mercaptoethanol (Sigma, St. Louis, MO) is added at $5 \times 10^{-5} \text{ M}$.

Serial dilutions of human interleukin-3 or fusion protein (hIL-3 mutein) are made in triplicate series in tissue culture medium supplemented as stated above in 96 well Costar 3596 tissue culture plates. Each well contained 50 μl of medium containing interleukin-3 or fusion protein once serial dilutions are completed. Control wells contained tissue culture medium alone (negative control). AML 193 1.3 cell suspensions prepared as above are added to each well by pipetting 50 μl (2.5×10^4 cells) into each well. Tissue culture plates are incubated at 37°C with 5% CO_2 in humidified

air for 3 days. On day 3, 0.5 μ Ci 3 H-thymidine (2 Ci/mM; New England Nuclear, Boston, MA) is added in 50 μ l of tissue culture medium. Cultures are incubated at 37°C with 5% CO₂ in humidified air for 18-24 hours. Cellular DNA is harvested onto glass filter mats (Pharmacia LKB, Gaithersburg, MD) using a TOMTEC cell harvester (TOMTEC, Orange, CT) which utilized a water wash cycle followed by a 70% ethanol wash cycle. Filter mats are allowed to air dry and then placed into sample bags to which scintillation fluid (Scintiverse II, Fisher Scientific, St. Louis, MO or BetaPlate Scintillation Fluid, Pharmacia LKB, Gaithersburg, MD) is added. Beta emissions of samples from individual tissue culture wells are counted in a LKB Betaplate model 1205 scintillation counter (Pharmacia LKB, Gaithersburg, MD) and data is expressed as counts per minute of 3 H-thymidine incorporated into cells from each tissue culture well. Activity of each human interleukin-3 preparation or fusion protein preparation is quantitated by measuring cell proliferation (3 H-thymidine incorporation) induced by graded concentrations of interleukin-3 or fusion protein. Typically, concentration ranges from 0.05 pM - 105 pM are quantitated in these assays. Activity is determined by measuring the dose of interleukin-3 or fusion molecule which provides 50% of maximal proliferation [EC₅₀ = 0.5 x (maximum average counts per minute of 3 H-thymidine incorporated per well among triplicate cultures of all concentrations of interleukin-3 tested - background proliferation measured by 3 H-thymidine incorporation observed in triplicate cultures lacking interleukin-3]. This EC₅₀ value is also equivalent to 1 unit of bioactivity. Every assay is performed with native interleukin-3 as a reference standard so that relative activity levels could be assigned.

Typically, the protein fusions were tested in a concentration range of 2000pM to 0.06pM titrated in serial 2 fold dilutions. Biological activity of the

fusion molecules was compared to the following standards as described below.

Protein fusions comprised in part of G-CSF, pMON3987, pMON3995, pMON3997, pMON26406, pMON26433, pMON26415, 5 pMON26416, and pMON26430, were compared to the dose response curve of equal molar concentrations of hG-CSF and pMON13288 or pMON13416.

10 Protein fusions comprised in part of GM-CSF, pMON3989 and pMON3998 were compared to the dose response curve of equal molar concentrations of hGM-CSF and pMON13288.

15 Protein fusions comprised of dimers of hIL-3 variants, pMON3988, pMON26425, pMON26427, pMON26420, pMON26429 and pMON26431 were compared to the dose response curve of pMON13288 or pMON13416.

20 15 Activity for each sample was determined by the concentration which gave 50% of the maximal response by fitting a four-parameter logistic model to the data. It was observed that the upper plateau (maximal response) for the sample and the standard with which it was compared did not differ. Therefore relative potency calculation for each sample was determined from EC50 estimations for the sample and the standard as indicated above. Relative potency (EC50 of standard divided by EC50 of sample) reported in Table 3 is the mean of at least two independent assays unless indicated.

25 AML 193.1.3 cells proliferate in response to hIL-3, hGM-CSF and hG-CSF. Therefore the following additional assays were performed for some samples to demonstrate that the G-CSF or GM-CSF portion of the fusion proteins was active. Proliferation assay was performed using neutralizing polyclonal antibodies to pMON13288. In addition, a fusion molecule with the factor Xa cleavage site was cleaved then purified and the halves of the molecule were assayed for proliferative activity. These 30 experiments showed that both components of the fusion protein were active.

Table 3 AML cell proliferation assay

pMON	R1	Linker	R2	AML 193.1.3 Bioactivity (relative potency)
pMON3987	13288	Linker 1	G-CSF	0.35 ±0.11
pMON3988	13288	Linker 1	13288	0.64 ±0.13
pMON3989	13288	Linker 1	GM-CSF	0.6 ±0.09
pMON3995	G-CSF	Linker 1	13288	0.41 ±0.44
pMON3997	13288	Linker 7	G-CSF	0.26 (n=1)
pMON3998	13288	Linker 7	GM-CSF	0.21 (n=1)
pMON26406	13288	Linker 4	G-CSF	0.37 ±0.30
pMON26433	G-CSF	Linker 4	13288	0.79 ±0.35
pMON26415	13288	Linker 1	G-CSF Ser17	0.46 ±0.08
pMON26416	G-CSF	Linker 1	13416	0.43 ±0.02
pMON26425	13288	Linker 2	13288	1.32 ±0.41
pMON26427	13288	Linker 3	13288	1.41 ±0.91
pMON26420	13416	Linker 1	13416	2.09 ±0.52
pMON26430	13288	Linker 6	G-CSF	1.04 ±0.69
pMON26429	13288	Linker 5	13288	1.88 ±0.09
pMON26431	13288	Linker 6	13288	0.66 ±0.26

Methylcellulose Assay

This assay provides a reasonable approximation of the
5 growth activity of colony stimulating factors to
stimulate normal bone marrow cells to produce different
types of hematopoietic colonies in vitro (Bradley et al.,
1966, Pluznik et al., 1965).

10 Methods

Approximately 30 ml of fresh, normal, healthy bone marrow
aspirate are obtained from individuals. Under sterile
conditions samples are diluted 1:5 with a 1X PBS
(#14040.059 Life Technologies, Gaithersburg, MD.)
15 solution in a 50 ml conical tube (#25339-50 Corning,
Corning MD). Ficoll (Histopaque 1077 Sigma H-8889) is
layered under the diluted sample and centrifuged, 300 x g
for 30 min. The mononuclear cell band is removed and
washed two times in 1X PBS and once with 1% BSA PBS
20 (CellPro Co., Bothel, WA). Mononuclear cells are counted
and CD34+ cells are selected using the Ceprate LC (CD34)
Kit (CellPro Co., Bothel, WA) column. This fractionation
is performed since all stem and progenitor cells within
the bone marrow display CD34 surface antigen.

25

Cultures are set up in triplicate with a final volume of
1.0 ml in a 35 X 10 mm petri dish (Nunc#174926).
Culture medium is purchased from Terry Fox Labs. (HCC-
4230 medium (Terry Fox Labs, Vancouver, B.C., Canada) and
30 erythropoietin (Amgen, Thousands Oaks, CA.) is added to
the culture media. 3,000-10,000 CD34+ cells are added
per dish. Native IL-3 and fusion molecules are added to
give final concentrations ranging from .001nM 10nM.
Native IL-3 and fusion molecules are supplied in house.
35 G-CSF (Neupogen) is from Amgen.
Cultures are resuspended using a 3cc syringe and 1.0 ml
is dispensed per dish. Control (baseline response)

cultures received no colony stimulating factors. Positive control cultures received conditioned media (PHA stimulated human cells: Terry Fox Lab. H2400). Cultures are incubated at 37°C, 5% CO₂ in humidified air.

5 Hematopoietic colonies which are defined as greater than 50 cells are counted on the day of peak response (days 10-11) using a Nikon inverted phase microscope with a 40x objective combination. Groups of cells containing fewer than 50 cells are referred to as clusters. Alternatively 10 colonies can be identified by spreading the colonies on a slide and stained or they can be picked, resuspended and spun onto cytocentrifuge slides for staining.

Human Cord Blood Hemopoietic Growth Factor Assays

15

Bone marrow cells are traditionally used for in vitro assays of hematopoietic colony stimulating factor (CSF) activity. However, human bone marrow is not always available, and there is considerable variability between donors. Umbilical 20 cord blood is comparable to bone marrow as a source of hematopoietic stem cells and progenitors (Broxmeyer et al., 1992; Mayani et al., 1993). In contrast to bone marrow, cord blood is more readily available on a regular basis. There is also a potential to reduce assay variability by pooling cells 25 obtained fresh from several donors, or to create a bank of cryopreserved cells for this purpose. By modifying the culture conditions, and/or analyzing for lineage specific markers, it should be possible to assay specifically for granulocyte / macrophage colonies (CFU-GM), for megakaryocyte CSF activity, or 30 for high proliferative potential colony forming cell (HPP-CFC) activity.

Methods

Mononuclear cells (MNC) are isolated from cord blood within 24 35 hr. of collection, using a standard density gradient (1.077g/ml Histopaque). Cord blood MNC have been further enriched for stem cells and progenitors by several procedures, including

immunomagnetic selection for CD14-, CD34+ cells; panning for SBA-, CD34+ fraction using coated flasks from Applied Immune Science (Santa Clara, CA); and CD34+ selection using a CellPro (Bothell, WA) avidin column. Either freshly isolated or 5 cryopreserved CD34+ cell enriched fractions are used for the assay. Duplicate cultures for each serial dilution of sample (concentration range from 1pM to 1204pM) are prepared with 1x10⁴ cells in 1ml of .9% methycellulose containing medium without additional growth factors (Methocult H4230 from Stem Cell Technologies, Vancouver, BC.). In some experiments, Methocult H4330 containing erythropoietin (EPO) was used instead of 10 Methocult H4230, or Stem Cell Factor (SCF), 50ng/ml (Biosource International, Camarillo, CA) was added. After culturing for 7-9 days, colonies containing >30 cells are counted. In order to 15 rule out subjective bias in scoring, assays are scored blind.

Analysis of c-mpl ligand proliferative activity

20

Methods

1. Bone marrow proliferation assay
 - a. CD34+ Cell Purification:
25 Between 15-20 ml bone marrow aspirates were obtained from normal allogeneic marrow donors after informed consent. Cells were diluted 1:3 in phosphate buffered saline (PBS, Gibco-BRL), 30 ml were layered over 15 ml Histopaque-1077 (Sigma) and centrifuged for 30 minutes at 300 RCF. The mononuclear interface layer was collected and washed in PBS. CD34+ cells were enriched from the mononuclear cell preparation using an affinity column per manufacturers instructions (CellPro, Inc, Bothell WA). After enrichment, the purity of CD34+ cells was 70% on 30 average as determined by using flow cytometric analysis using anti CD34 monoclonal antibody conjugated to fluorescein and anti CD38 conjugated to phycoerythrin (Becton Dickinson, San Jose CA).

Cells were resuspended at 40,000 cells/ml in X-Vivo 10 media (Bio-Whittaker, Walkersville, MD) and 1 ml was plated in 12-well tissue culture plates (Costar). The growth factor rhIL-3 was added at 100 ng/ml (pMON5873) was added to some wells. hIL3 variant, pMON13288, was used at 10 ng/ml or 100 ng/ml. Conditioned media from BHK cells transfected with plasmid encoding c-mpl ligand were tested by addition of 100 µl of supernatant added to 1 ml cultures (approximately a 10% dilution). Cells were incubated at 37°C for 8-14 days at 5% CO₂ in a 37°C humidified incubator.

b. Cell Harvest and Analysis:

At the end of the culture period a total cell count was obtained for each condition. For fluorescence analysis and ploidy determination cells were washed in megakaryocyte buffer (MK buffer, 13.6 mM Sodium Citrate, 1 mM Theophylline, 2.2 µM PGE1, 11 mM Glucose, 3% w/v BSA, in PBS, pH 7.4,) [Tomer et al., (1987)] resuspended in 500 µl of MK buffer containing anti-CD41a FITC antibody (1:200, AMAC, Westbrook, ME) and washed in MK buffer. For DNA analysis cells were permeabilized in MK buffer containing 0.5% Tween 20 (Fisher, Fair Lawn NJ) for 20 min. on ice followed by fixation in 0.5% Tween-20 and 1% paraformaldehyde (Fisher Chemical) for 30 minutes followed by incubation in Propidium Iodide (Calbiochem, La Jolla CA) (50 µg/ml) with RNA-ase (400 U/ml) in 55% v/v MK buffer (200mOsm) for 1-2 hours on ice. Cells were analyzed on a FACScan or Vantage flow cytometer (Becton Dickinson, San Jose, CA). Green fluorescence (CD41a-FITC) was collected along with linear and log signals for red fluorescence (PI) to determine DNA ploidy. All cells were collected to determine the percent of cells that were CD41+. Data analysis was performed using software by LYSIS (Becton Dickinson, San Jose, CA). Percent of cells expressing the CD41 antigen was obtained from flow cytometry analysis(Percent). Absolute (Abs) number of

150

CD41+ cells/ml was calculated by: (Abs)=(Cell Count)*(Percent)/100.

2. Megakaryocyte fibrin clot assay.

5

CD34+ enriched population were isolated as described above. Cells were suspended at 25,000 cells/ml with/without cytokine(s) in a media consisting of a base Iscoves IMDM media supplemented with 0.3% BSA, 0.4mg/ml apo-transferrin, 6.67 μ M FeCl₂, 25 μ g/ml CaCl₂, 25 μ g/ml L-asparagine, 500 μ g/ml E-amino-n-caproic acid and Penicillin/Streptomycin. Prior to plating into 35mm plates, thrombin was added (0.25 Units/ml) to initiate clot formation. Cells were incubated at 37°C for 13 days 15 at 5% CO₂ in a 37°C humidified incubator.

At the end of the culture period plates were fixed with Methanol:Acetone (1:3), air dried and stored at -200C until staining. A peroxidase immunocytochemistry 20 staining procedure was used (Zymed, Histostain-SP. San Francisco, CA) using a cocktail of primary monoclonal antibodies consisting of anti CD41a, CD42 and CD61. Colonies were counted after staining and classified as negative, CFU-MK (small colonies, 1-2 foci and less than 25 approx. 25 cells), BFU-MK (large, multi-foci colonies with > 25 cells) or mixed colonies (mixture of both positive and negative cells).

Example 70

30 Administration of hIL-3 variant, pMON13288, and c-mpl ligand fusion molecule has a more than additive effect on megakaryocyte expansion than either cytokine alone.

35 Megakaryocyte fibrin clot cultures were set up as described in methods section. pMON26448 is the 1-153 amino acid form of c-mpl ligand (Meg-CSF). pMON26463 is a fusion molecule consisting of hIL3 variant, pMON13288

and the 1-153 amino acid form of c-mpl ligand. Incubation in the presence of hIL3 variant, pMON13288 gave rise to colonies that were predominantly negative for megakaryocyte markers (86/114, (Table 4)) except for 5 number of small CFU-MK colonies (23/114). pMON26448 alone gave rise primarily to CFU-MK colonies (172/175) with only a few number of negative colonies (3/175). Combination of hIL3 variant, pMON13288 and pMON26448 gave 10 arise to a large number of positive colonies (295/414) that were predominantly of the BFU-MK morphology. There were a negative colonies as well (119/414). Total number 15 of positive colonies with co-administration was more than additive than with either cytokine alone. pMON26463, the fusion molecule gave results similar to the combination of hIL3 variant, pMON13288 and pMON26448. The number of negative cells is less than with hIL3 variant, pMON13288 which is probably due to a lower concentration of pMON13288 in the preparation (approximately 10ng/ml as part of the fusion molecule vs. 100ng/ml of hIL3 variant, 20 pMON13288)

Table 4.

Cytokine treatment	Colonies/Well					Total
	Negative	CFU-MK	BFU-MK	Mixed		
pMON13288	86	23	0	5	114	
pMON26448	3	73	98	1	175	
pMON26448 + pMON13288	119	29	244	22	414	
pMON26463	10	30	165	17	222	
Cytokine treatment	Colonies/100,000 plated					Total
	Negative	CFU-MK	BFU-MK	Mixed		
pMON13288	344	92	0	20	456	
pMON26448	12	292	392	4	700	
pMON26448 + pMON13288	476	116	976	88	1656	

152

pMON26463	40	120	660	68	888
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IL-3 Mediated Sulfidoleukotriene Release from Human Mononuclear Cells

The following assay is used to measure IL-3 mediated
5 sulfidoleukotriene release from human mononuclear cells.

Heparin-containing human blood is collected and layered onto an equal volume of Ficoll-Paque (Pharmacia # 17-0840-02) ready to use medium (density 1.077 g/ml.). The
10 Ficoll is warmed to room temperature prior to use and clear 50 ml polystyrene tubes are utilized. The Ficoll gradient is spun at 300 x g for 30 minutes at room temperature using a H1000B rotor in a Sorvall RT6000B refrigerated centrifuge. The band containing the
15 mononuclear cells is carefully removed, the volume adjusted to 50 mls with Dulbecco's phosphate-buffered saline (Gibco Laboratories cat. # 310-4040PK), spun at 400 x g for 10 minutes at 4°C and the supernatant is carefully removed. The cell pellet is washed twice with
20 HA Buffer [20 mM Hepes (Sigma # H-3375), 125 mM NaCl (Fisher # S271-500), 5 mM KCl (Sigma # P-9541), 0.5 mM glucose (Sigma # G-5000), 0.025% Human Serum Albumin (Calbiochem # 126654) and spun at 300 x g, 10 min., 4°C. The cells are resuspended in HACM Buffer (HA buffer
25 supplemented with 1 mM CaCl₂ (Fisher # C79-500) and 1 mM MgCl₂ (Fisher # M-33) at a concentration of 1 x 10⁶ cells/ml and 180 µl are transferred into each well of 96 well tissue culture plates. The cells are allowed to acclimate at 37°C for 15 minutes. The cells are primed by
30 adding 10 µls of a 20 X stock of various concentrations of cytokine to each well (typically 100000, 20000, 4000, 800, 160, 32, 6.4, 1.28, 0 fM IL3). The cells are incubated for 15 minutes at 37°C. Sulfidoleukotriene release is activated by the addition of 10 µls of 20 X (1000 nM) fmet-leu-phe (Calbiochem # 344252) final concentration 50nM FMLP and incubated for 10 minutes at
35

- 37°C. The plates are spun at 350 x g at 4°C for 20 minutes. The supernatants are removed and assayed for sulfidoleukotrienes using Cayman's Leukotriene C4 EIA kit (Cat. #420211) according to manufacturers' directions.
- 5 Native hIL-3 is run as a standard control in each assay.

Further details known to those skilled in the art may be found in T. Maniatis, et al. Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory (1982) and references cited therein, incorporated herein by reference; and in J. Sambrook, et al., Molecular Cloning, A Laboratory Manual, 2nd edition, Cold Spring Harbor Laboratory (1989) and references cited therein, incorporated herein by reference.

15

Additional details on the IL-3 variants of the present invention may be found in co-pending United States Patent Application Serial number PCT/US93/11197 which is hereby incorporated by reference in its entirety as if written herein.

Additional details on how to make the fusion protein can be found in WO 92/04455 and WO 91/02754.

Additional details about the lymphokine and the variants thereof can be found in U.S. Patent 4,810,643, and 5,218,092 E.P. Application 02174004.

All references, patents or applications cited herein are incorporated by reference in their entirety as if written herein.

30 Amino acids are shown herein by standard one letter or three letter abbreviations as follows:

	Abbreviated Designation	Amino Acid
35	A	Ala
	C	Cysteine
	D	Aspartic acid

154

	E	Glu	Glutamic acid
	F	Phe	Phenylalanine
	G	Gly	Glycine
	H	His	Histidine
5	I	Ile	Isoleucine
	K	Lys	Lysine
	L	Leu	Leucine
	M	Met	Methionine
	N	Asn	Asparagine
10	P	Pro	Proline
	Q	Gln	Glutamine
	R	Arg	Arginine
	S	Ser	Serine
	T	Thr	Threonine
15	V	Val	Valine
	W	Trp	Tryptophan
	Y	Tyr	Tyrosine

20

TABLE 5
OLIGONUCLEOTIDES

25	88CTERM1.REQ Length: 000041 AATTCCGGGA AAAACTGACG TTCTATCTGG TTACCCCTTGA G [SEQ ID NO:91]
30	88CTERM4.REQ Length: 000046 CTGCGCTTGC TCAAGGGTAA CCAGATAGAA CGTCAGTTTT TCCCCG [SEQ ID NO:92]
35	88XA2.REQ Length: 000039 CAAGCGCAGG AACAACAGTA CGTAATCGAG GGAAGGATT [SEQ ID NO:93]
40	88XA5.REQ Length: 000039 ACCCGGGGAA ATCCTTCCCT CGATTACGTA CTGTTGTTC [SEQ ID NO:94]
45	GLYN3.REQ Length: 000063 TCCCCCCGTG GTGGTTCTGG CGGGGGCTCC AACATGTAAG GTACCGCATG CAAGCTTAGA TCT [SEQ ID NO:95]
	GLYN6.REQ Length: 000058

155

AGCTAGATCT AAGCTTGCAT GCGGTACCTT ACATGTTGGA GCGGCCGCCA
GAACCACC [SEQ ID NO:96]

5 IGG2B1.REQ Length: 000074

CCGGGTGAAC CGTCTGGTCC AATCTCTACT ATCAACCCGT CTCTCCGTC
TAAAGAACATCT CATAAAATCTC CAAA [SEQ ID NO:97]

10 IGG2B2.REQ Length: 000074

CATGTTTGGA GATTTATGAG ATTCTTTAGA CGGAGGAGAC GGGTTGATAG
TAGAGATTGG ACCAGACGGT TCAC [SEQ ID NO:98]

15 GCSFSNA1.REQ Length: 000068

CTAGCCATCT GCAGAGCTTC CTGGAGGTGT CGTACCGCGT TCTACGCCAC
CTTGCAGC CCTACGTA [SEQ ID NO:99]

20 GCSFSNA2.REQ Length: 000068

AGCTTACGTA GGGCTGCGCA AGGTGGCGTA GAACGCGGTGA CGACACCTCC
AGGAAGCTCT GCAGATGG [SEQ ID NO:100]

25 LYSXA1.REQ Length: 000021

GTAATCGAGG GAAAGATTTC C [SEQ ID NO:101]

LYSX A2.REQ Length: 000025

30 CCGGGGAAAT CTTTCCCTCG ATTAC [SEQ ID NO:102]

GLYXA1.REQ Length: 000021

35 GTAGAGGGCG GTGGAGGCTC C [SEQ ID NO:103]

GLYXA2.REQ Length: 000025

CCGGGGAGCC TCCACCGCCC TCTAC [SEQ ID NO:104]

40 GM-AUP.REQ Length: 000058

CATGGCACCA GCAAGATCAC CATCACCATC AACTCAACCT TGGAACATG
TGAATGCC [SEQ ID NO:105]

45 GM-ALOW.REQ Length: 000052

CATTCACATG TTCCCAAGGT TGAGTTGATG GTGATGGTGA TCTTGCTGGT
GC [SEQ ID NO:106]

50 G-CYS18.REQ Length: 000066

CTGCCAGCTC CCTGCCAG AGCTTCCTGC TCAAGTCCTT AGACCAAGTG
AGGAAGATCC AGGGCG [SEQ ID NO:107]

55 GCYS18LO.REQ Length: 000066

CTGGATCTTC CTCACTTGCT CTAAAGACTT GAGCAGGAAG CTCTGGGCA
GGGAGCTGGC AGGGCC [SEQ ID NO:108]

60 HIL6231.REQ Length: 000048

156

AGCTTACCTG CCATGGCTCC AGTACCACCA GGTGAAGATT CCAAAGAT
[SEQ ID NO:109]

5 HIL6232.REQ Length: 000040

TTGGAATCTT CACCTGGTGG TACTGGAGCC ATGGCAGGTA [SEQ ID NO:110]

10 HGCSFMA1.REQ Length: 000026

AGCTTCCATG GCTACCCCCC TGGGCC [SEQ ID NO:111]

HGCSFMA2.REQ Length: 000018

15 CAGGGGGGTA GCCATGGA [SEQ ID NO:112]

HGCSFAT1.REQ Length: 000020

20 CATGGCTACA CCATTGGGCC [SEQ ID NO:113]

HGCSFAT2.REQ Length: 000012

CAATGGTGTA GC [SEQ ID NO:114]

25 HGCSFAT3.REQ Length: 000020

CATGGCTACA CCATTAGGAC [SEQ ID NO:115]

30 HGCSFAT4.REQ Length: 000012

TAATGGTGTA GC [SEQ ID NO:116]

PREFOR.REQ

35 CCTGTCAACC CGGGCGGCCGG CTCTGGTGGT [SEQ ID NO:117]

REVPRE.REQ

40 TCATAATACA TGTTACCGGA ACGGAGCCGC C [SEQ ID NO:118]

FORXTRA.REQ

ATCGTCTGAC CTCCGGGAC CTCCTGTCAA TGCT [SEQ ID NO:119]

45 XTRAREV.REQ

AGCGTTTGAC ATGTTTCAT AATCAAAATC [SEQ ID NO:120]

50 c-mplNcoI

ACGTCCATGGCNTCNCCNGNCNNCTGCTTGTGACCTCCGAGTC [SEQ ID NO:169]
(where N= G, C, T or A)

55 c-mplEcoRI

AATAGCTGAATTCTTACCCCTCCTGAGACAGATT [SEQ ID NO:170]

c-mplHindIII

60 TGACAAGCTTACCTGACGCAGAGGGTGGACCCT [SEQ ID NO:171]

157

Eco-mpl

ATGCACGAATTCCCTGACGCAGAGGGTGG [SEQ ID NO:172]

5

EcoSnaI

AATTCCATGCATAC [SEQ ID NO:173]

10

ECOSNA2

GGTACGTATG [SEQ ID NO:174]

15

TABLE 6DNA SEQUENCES

PMON13023

20 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 25 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCTATGCTGTC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 30 TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 GGGAAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
 35 CACCATTAGG CCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTGC
 TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
 GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
 40 GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGGCCAG
 CCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT
 45 CTACCAGGGG CCTCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
 CCACCTTGGA CACACTGCAG CTGGACGTG CCGACTTTGC CACCACCATC
 TAATCTGGAA TGGGCCCCCTGC CCTGCAGCCC ACCCAGGGTG CCATGCCGGC
 50 CTTCGCCTCT CCTTTCCAGC GCCGGGCAGG AGGGGTCCCTG GTTGCTAGCC
 ATCTGCAGAG CCTCCCTGGAG GTGTCGTACG GCGTTCTACG CCACCTTGCG
 55 CAGCCC [SEQ ID NO:53]

PMON13021

158

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 5 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 10 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 15 GGGAGGATT TCCCCGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
 ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
 AACCCCTTGC TGGACCCGAA CAACCTCAAT TCTGAAGACA TGGATATCCT
 20 GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTC GTAAGGGCTG
 TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
 25 CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
 CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC
 TGTTACCCCT TGAGCAAGCG CAGGAACAAC AG [SEQ ID NO:54]
 30

pMON13022

35 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 40 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 45 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 GGGAGGATT TCCCCGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCAC
 50 CGGCTCGTTC CCCGTCCCCG TCTACCCAGC CGTGGGAACA CGTGAATGCC
 ATCCAGGAGG CCCGGCGTCT CCTGAACCTG ACTAGAGACA CTGCTGCTGA
 55 GATGAATGAA ACAGTAGAAG TGATATCAGA AATGTTGAC CTCCAGGAGC
 CGACTTGCCT ACAGACCCGC CTGGAGCTGT ACAAGCAGGG CCTGCGGGGC
 AGCCTCACCA AGCTCAAGGG CCCCTTGACC ATGATGCCA GCCACTACAA
 60

159

GCAGCACTGC CCTCCAACCC CGGAAACTTC CTGTGCAACC CAGATTATCA
 CCTTTGAAG TTTCAAAGAG AACCTGAAGG ACTTCCTGCT TGTCATCCCC
 5 TTTGACTGCT GGGAGCCAGT CCAGGAG [SEQ ID NO:55]

pMON13039

10 ATGGCTTAAC GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 15 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 20 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTG A GCAAGCGCAG GAACAACAGT ACGTAATCGA
 25 GGGAAAGGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
 CACCAATTGGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT
 TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
 30 GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
 GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
 35 GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCT
 CTACCAGGGG CCTCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
 CCACCTTGGG CACACTGCAG CTGGACGTG CCGACTTTGC CACCACCATC
 40 TGGCAGCAGA TGGAAAGAACT GGGAAATGGCC CCTGCCCTGC AGCCCACCCA
 GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGGCCGG GCAGGGAGGGG
 TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT
 45 CTACGCCACC TTGCGCAGCC C [SEQ ID NO:56]

pMON13049

50 ATGGCTTAAC GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 55 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 60

160

CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACCTAATCGA
 5 GGGAAAGGATT TCCCCGGGTG GTGGTTCTGG CGGGCGCTCC AACATGGCTC
 CAGTACCACC AGGTGAAGAT TCCAAAGATG TGGCCGCCCG ACACAGACAG
 10 CCACTCACCT CTTCAAGAACG AATTGACAAA CAAATCGGT ACATCCTCGA
 CGGGATATCA GCCCTGAGAA AGGAGACATG TAACAAGAGT AACATGTGTG
 AAAGCAGCAA AGAGGCCTA GCAGAAAACA ACCTGAACCT TCCAAAGATG
 15 GCTGAAGAAAG ATGGATGCTT CCAATCCGGA TTCAATGAGG AGACTTGCGCT
 GGTGAAATC ATCACTGGTC TTTTGGAGTT TGAGGTATAAC CTCGAGTAC
 20 TCCAGAACAG ATTTGAGACT AGTGAGGAAC AAGCCAGAGC TGTGCAGATG
 TCGACAAAAG TCCTGATCCA GTTCCTGCAG AAAAAGGCAA AGAATCTAGA
 TGCAATAACC ACCCCTGACC CAACCACAAA TGCACTCCCTG CTGACGAAGC
 25 TGCAGGCACA GAACCAGTGG CTGCAGGACA TGACAACCTCA TCTCATTCTG
 CGCAGCTTTA AGGAGTTCCCT GCAGTCCAGC CTGAGGGCTC TTCGGCAAAT
 30 G [SEQ ID NO:57]

PMON13055

ATGGCTTAACG GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 35 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGCTA
 40 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 45 TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACCTAATCGA
 GGGAAAGATT TCCCCGGGTG GTGGTTCTGG CGGGCGCTCC AACATGGCTA
 50 ACTGCTCTAT AATGATCGAT GAAATTATAAC ATCACTTAAAGAGACCACCT
 AACCCCTTGCA TGGACCCGAA CAACCTCAAT TCTGAAGACA TGGATATCCT
 GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCCGATTC GTAAGGGCTG
 55 TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
 CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
 60 CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC

TGGTTACCT TGAGCAAGCG CAGGAACAAC AG [SEQ ID NO:58]

5 pMON13054

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 10 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 ACGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 15 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 20 GGGAAAGATT TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA
 CACCATTGGG CCCTGCCAGC TCCCTGCCCT AGAGCTTCCT GCTCAAGTCT
 25 TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
 GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
 GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
 30 GCCCTGCAGC TGGCAGGCTG CTTGAGCAA CTCCATAGCG GCCTTTTCCT
 CTACCAAGGGG CTCCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
 35 CCACCTTGGG CACACTGCAG CTGGACGTCG CCGACTTTGC CACCACCATC
 TGGCAGCAGA TCGAAGAACT GGGAAATGGCC CCTGCCCTGC AGCCCACCCA
 40 GGGTGCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG GCAGGAGGGG
 TCCTGGTTGC TAGCCATCTG CAGAGCTTC TGGAGGTGTC GTACCGCGTT
 CTACGCCACC TTGCGCAGCC C [SEQ ID NO:59]

45

pMON13056

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 50 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 ACGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 55 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 60

162

TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
 CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGGC GGCTCC AACATGGCTA
 5 CACCATTGGG CCCTGCCAGC TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT
 TTAGAGCAAG TGACCCAAGAT CCAGGGCGAT GGCGCAGCGC TCCAGGAGAA
 10 GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG GTGCTGCTCG
 GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG
 GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTTCCCT
 15 CTACCAGGGG CTCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGGTC
 CCACCTTGGA CACACTGCAG CTGGACGTG CCGACTTTGC CACCACCATC
 20 TGGCAGCAGA TGGAAGAACT GGGAAATGGCC CCTGCCCTGC AGCCCACCCA
 GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG GCAGGAGGGG
 TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT
 25 CTACGCCACC TTGGCAGCC C [SEQ ID NO:60]

pMON13057

30 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 35 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGCTGTC CCTCTGCCAC GGCCGCACCC TCTCGACATC
 40 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
 CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGGC GGCTCC AACATGGCTA
 45 ACTGCTCTAT AATGATCGAT GAAATTATAC ATCACTTAAA GAGACCACCT
 AACCTTTGC TGGACCCGAA CAACCTCAAT TCTGAAGACA TGGATATCCT
 50 GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTG GTAAGGGCTG
 TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC
 55 CAACCAGTGC TGCCCTGTC CACGGCCGCA CCCTCTCGAC ATCCAATCAT
 CATCAAGGCA GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC
 TGGTTACCCCT TGAGCAAGCG CAGGAACAAAC AG [SEQ ID NO:61]

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PMON13036

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 5 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 10 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 15 TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 .GGGAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 20 CGTCTCCTCC GTCTAAAGAA TCTCATAAAAT CTCCAAACAT GGCTAACTGC
 TCTATAATGA TCGATGAAAT TATAACATCAC TTAAAGAGAC CACCTAACCC
 TTTGCTGGAC CCGAACAAACC TCAATTCTGA AGACATGGAT ATCCTGATGG
 25 AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG
 CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTCGTA ATCTCCAACC
 ATGTCTGCCCT TCTGCCACGG CGCGACCCCTC TCGACATCCA ATCATCATCA
 30 AGGCAGGTGA CTGGCAAGAA TTCCGGAAA AACTGACGTT CTATCTGGTT
 ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:62]
 35

PMON13059

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 40 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 45 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 GGGAAAGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 CGTCTCCTCC GTCTAAAGAA TCTCATAAAAT CTCCAAACAT GGCTAACTGC
 50 TCTATAATGA TCGATGAAAT TATAACATCAC TTAAAGAGAC CACCTAACCC
 TTTGCTGGAC CCGAACAAACC TCAATTCTGA AGACATGGAT ATCCTGATGG
 55 AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG
 60

164

5 CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTCGTA ATCTCCAACC
 AGTGTCTGCC 5 TCTGCCACGG CGGCACCCCTC TCGACATCCA ATCATCATCA
 AGGCAGGTGA CTGGCAAGAA TTCCGGAAA AACTGACGTT CTATCTGGTT
 ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:63]

10 pMON13061

15 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT 15 GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTCG
 TAATCTCAA 20 CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG 25 TTACCCCTGA GCAAGCGCAG GAACAACAGT ACCTAGAGGG
 CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 CGTCTCCTCC 30 GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTAACTGC
 TCTATAATGA TCGATGAAAT TATACATCAC TTAAAGAGAC CACCTAACCC
 TTTGCTGGAC CCGAACAAACC TCAATTCTGA AGACATGGAT ATCCTGATGG
 AACGAAACCT 35 TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG
 CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTCGTA ATCTCCAACC
 ATGTCTGCC 40 TCTGCCACGG CGGCACCCCTC TCGACATCCA ATCATCATCA
 AGGCAGGTGA CTGGCAAGAA TTCCGGAAA AACTGACGTT CTATCTGGTT
 ACCCTTGAGC AAGCGCAGGA ACAACAG [SEQ ID NO:64]

45 pMON13062

50 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT 55 GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTCG
 TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT 60 CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACCTAGAGGG

165

5 GGGAAGGATT TCCCCCGGGC CTCCGTCAA TGCTGGCGGC GGCTCTGGTG
 GTGGTTCTGG TGGCGGCTCT GAGGGTGGCG GCTCTGAGGG TGGCGGTTCT
 GAGGGTGGCG GCTCTGAGGG TGGCGGTTCC GGTGGCGGCT CCGGTTCCGG
 TGATTTGAT TATGAAAACA TGGCTACACC ATTGGGCCCT GCCAGCTCCC
 10 TCCCCCAGAG CTTCTGCTC AAGTCTTAG AGCAAGTGAG GAAGATCCAG
 GGCAGATGGCG CAGCGCTCCA GGAGAAGCTG TGTGCCACCT ACAAGCTGTG
 15 CACCCCCGAG GAGCTGGTGC TGCTCGGACA CTCTCTGGC ATCCCCCTGGG
 CTCCCCCTGAG CTCCGTCCCC AGCCAGGCC TGCAGCTGGC AGGCTGCTTG
 AGCCAACCTCC ATAGCGGCCT TTTCCTCTAC CAGGGGCTCC TGCAGGCCCT
 20 GGAAGGGATA TCCCCCGAGT TGGGTCCCAC CTTGGACACA CTGCAGCTGG
 ACGTCGCCGA CTTTGCCACC ACCATCTGGC AGCAGATGGA AGAACTGGGA
 25 ATGGCCCCCTG CCCTGCAGCC CACCCAGGGT GCCATGCCGG CCTTCGCCTC
 TGCTTTCCAG CGCCGGGCAG GAGGGGTCCT GGTTGCTAGC CATCTGCAGA
 GCTTCCTGGA GGTGTCGTAC CGCGTTCTAC GCCACCTTGC GCAGCCC
 30 [SEQ ID NO:65]

PMON13031

35 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 40 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 45 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 GCGAAGGATT TCCCCCGGGC CTCCGTCAA TGCTGGCGGC GGCTCTGGTG
 GTGGTTCTGG TGGCGGCTCT GAGGGTGGCG GCTCTGAGGG TGGCGGTTCT
 GAGGGTGGCG GCTCTGAGGG TGGCGGTTCC GGTGGCGGCT CCGGTTCCGG
 TGATTTGAT TATGAAAACA TGGCACCGGC TCGTTCCCCG TCCCCGTCTA
 50 55 CCCAGCCGTG GGAACACGTG AATGCCATCC AGGAGGGCCCG GCGTCTCCTG
 AACCTGAGTA GAGACACTGC TGCTGAGATG AATGAAACAG TAGAAGTGAT
 ATCAGAAATG TTTGACCTCC AGGAGCCGAC TTGCCTACAG ACCCGCCTGG
 60

166

AGCTGTACAA GCAGGGCCTG CGGGGCAGCC TCACCAAGCT CAAGGGCC
 TTGACCATGA TGGCCAGCCA CTACAAGCAG CACTGCCCTC CAACCCCCGG
 5 AACTTCCTGT GCAACCCAGA TTATCACCTT TGAAAGTTTC AAAGAGAAC
 TGAAGGACTT CCTGCTTGTC ATCCCCTTG ACTGCTGGGA GCCAGTCCAG
 10 GAG [SEQ ID NO:66]

PMON15937

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 15 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 20 AGGGCTTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCAA CCATGTCCTGC CCTCTGCCAC GGCGCGACCC TCTCGACATC
 25 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT' ACGTAATCGA
 GGGAGGATT TCCCCCGGTG GCGGCGGCTC TGGTGGTGGT TCTGGTGGCG
 30 GCTCTGAGGG TGGCGGCTCT GAGGGTGGCG GTTCTGAGGG TGGCGGCTCT
 GAGGGTGGCG GTTCCGGTGG CGGCTCCGGT TCCGGTAACA TGGCTACACC
 35 ATTAGGCCCT GCCAGCTCCC TGCCCCAGAG CTTCTGCTC AAGTGCTTAG
 AGCAAGTGAG GAAGATCCAG GGCGATGGCG CAGCGCTCCA GGAGAAGCTG
 TGTGCCACCT ACAAGCTGTG CCACCCCGAG GAGCTGGTGC TGCTCGGACA
 40 CTCTCTGGGC ATCCCCTGGG CTCCCTGAG CTCCCTGCCCT AGCCAGGGCC
 TGCAGCTGGC AGGCTGCTTG AGCCAACCTCC ATAGCGGCCT TTTCTCTAC
 45 CAGGGGCTCC TGCAGGGCCT GGAAGGGATA TCCCCCGAGT TGGGTCCCAC
 CTTGGACACA CTGCAGCTGG ACGTGGCCGA CTTTGCCACC ACCATCTGGC
 AGCAGATGGA AGAACTGGGA ATGGCCCCCTG CCCTGCAGCC CACCCAGGGT
 50 GCCATGCCGG CCTTCGCCCTC TGCTTTCCAG CGCCGGGCAG GAGGGGTCC
 GGTGCTAGC CATCTGCAGA GCTTCCTGGA GGTGTCGTAC CGCGTTCTAC
 55 GCCACCTTGCG GCAGCCC [SEQ ID NO:67]

PMON13034

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 60

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ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCTGA
 5 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCC
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGGCACCC TCTCGACATC
 10 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 GGGAAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 15 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
 TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC TTCCCTGCTCA AGTGCTTAGA
 20 GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
 GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
 TCTCTGGGCA TCCCCCTGGGC TCCCCCTGAGC TCCCTGCCCCA GCCAGGGCCCT
 25 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCCTCTACC
 AGGGGCTCCT GCAGGGCCCTG GGGATAT CCCCCCGAGTT GGGTCCCACC
 30 TTGGACACAC TGCAGCTGGA CCGAC TTTGCCACCA CCATCTGGCA
 GCAGATGGAA GAACTGGAA TGGCCCTGC CCTGCAGCCC ACCCAGGGTG
 CCATGCCGGC CTTGCCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCCTG
 35 GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG
 CCACCTTGCG CAGCCC [SEQ ID NO:68]

40

PMON13035

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 45 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTCTGA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCC
 50 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 GGGAAAGGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 55 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTAAACAT GGCAACGGCT
 60

168

CGTTCCCCGT CCCCCTCTAC CCAGCCGTGG GAACACGTGA ATGCCATCCA
 GGAGGCCCCGG CGTCTCCTGA ACCTGAGTAG AGACACTGCT GCTGAGATGA
 5 ATGAAACAGT AGAAGTGATA TCAGAAATGT TTGACCTCCA GGAGCCGACT
 TGCCTACAGA CCCGCCTGGA GCTGTACAAG CAGGGCCTGC GGGGCAGCCT
 10 CACCAAGCTC AAGGGCCCT TGACCATGAT GGCCAGCCAC TACAAGCAGC
 ACTGCCCTCC AACCCCCGAA ACTTCCTGTG CAACCCAGAT TATCACCTTT
 GAAAGTTTCA AAGAGAACCT GAAGGACTTC CTGCTTGTCA TCCCCTTTGA
 15 CTGCTGGGAG CCAGTCCAGG AG [SEQ ID NO:69]

PMON13058

20 ATGGCTTAAC GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 25 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
 TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC TCTCGACATC
 30 CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
 TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA
 35 GGGAAAGATT TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 CGTCTCCTCC GTCTAAAGAA TCTCATAAAAT CTCCAAACAT GGCTACACCA
 TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC TTCCCTGCTCA AGTGCTTAGA
 40 GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
 GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
 45 TCTCTGGGCA TCCCCGGGC TCCCCGTAGC TCCTGCCCA GCCAGGCCCT
 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGGCCCTT TTCCCTCTACC
 AGGGGCTCCT GCAGGCCCTG GAAGGGATAT CCCCCGAGTT GGGTCCCACC
 50 TTGGACACAC TGCAGCTGGA CGTCGCCGAC TTTGCCACCA CCATCTGGCA
 GCAGATGGAA GAACTGGAA TGGCCCTGC CCTGCAGCCC ACCCAGGGTG
 55 CCATGCCGGC CTTCGCCTCT GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG
 GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG
 CCACCTTGGCG CAGCCC [SEQ ID NO:70]

PMON13060

5 ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
 ACCACCTAAC CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG
 ATATCCTGAT GGAACGAAAC CTTCGAACTC CAAACCTGCT CGCATTGTA
 10 AGGGCTGTCA AGCACTTAGA AAATGCATCA GGTATTGAGG CAATTCTCG
 TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
 CAATCATCAT CAAGGCAGGT CTTGGCAAG AATTCCGGGA AAAACTGACCG
 15 TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
 CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
 20 CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTACACCA
 TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC TTCTGCTCA AGTGCTTAGA
 GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG GAGAAGCTGT
 25 GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTCGGACAC
 TCTCTGGGCA TCCCCCTGGC TCCCCCTGAGC TCCTGCCCCA GCCAGGCCCT
 30 GCAGCTGGCA GGCTGCTTGA GCCAACTCCA TAGCGCCCTT TTCCCTCTACC
 AGGGGCTCCT GCAGGCCCTG GAAGGGATAT CCCCCGAGTT GGGTCCCACC
 35 TTGGACACAC TGCAGCTGGA CGTCGCCGAC TTTGCCACCA CCATCTGGCA
 GCAGATGGAA GAACTGGAA TGGCCCCCTGC CCTGCAGCCC ACCCAGGGTG
 CCATGCCGGC TTTCGCTCT GCTTTCAGC GCCGGGCAGG AGGGGTCTG
 40 GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG
 CCACCTTGCG CAGCCC [SEQ ID NO:71]

45

PMON13026

50 ATGGCTACAC CATTAGGCCCT TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
 CAAGTGCTTA GACCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
 AGGAGAAAGCT GTGTGCCACC TACAAGCTGT GCCACCCGA GGAGCTGGTG
 55 CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG GCTCCCTGA GCTCCTGCC
 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
 TTTTCCCTCTA CCAGGGGCTC CTGCAGGCCCT TGGAAAGGGAT ATCCCCCGAG
 60 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTGCCCG ACTTTGCCAC

170

5 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC
 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTCCA GCGCCGGGCA
 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
 CGCGTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATT
 10 CCCCGGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA
 ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTA ACCCTTGCT
 GGACCCGAAC AACCTCAATT CTGAAGACAT GGATATCCTG ATGAAACGAA
 15 ACCTTCGAAC TCCAAACCTG CTCGCATTG TAAGGGCTGT CAAGCACTTA
 GAAAATGCAT CAGGTATTGA GGCAATTCTT CGTAATCTCC AACCATGTCT
 20 GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC ATCAAGGCAG
 GTGACTGGCA AGAATTCCGG GAAAAACTGA CGTTCTATCT GGTTACCCCT
 25 GAGCAAGCGC AGGAACAACA G [SEQ ID NO:72]

PMON13063

30 ATGGCTACAC CATTAGGCCG TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
 CAAAGTCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
 AGGAGAACGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
 35 CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG GCTCCCTGA GCTCCCTGCC
 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
 TTTTCCTCTA CCAGGGCTC CTGCAGGCCG TGGAAGGGAT ATCCCCCGAG
 40 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC
 45 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTCCA GCGCCGGGCA
 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
 CGCGTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATT
 50 CCCCGGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCCTCCG
 TCTAAAGAAT CTCATAAACATC TCCAAACATG GCTAACTGCT CTATAATGAT
 55 CGATGAAATT ATACATCACT TAAAGAGACC ACCTAACCTT TTGCTGGACC
 CGAACAAACCT CAATTCTGAA GACATGGATA TCCTGATGGA ACGAACCTT
 CGAACACTCCAA ACCTGCTCGC ATTCTGTAAGG GCTGTCAAGC ACTTAGAAAA
 60

171

TGCATCAGGT ATTGAGGCAA TTCTTCGTAAC TCTCCAACCA TGTCTGCCCT
 CTGCCACGGC CGCACCCCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC
 5 TGGCAAGAAT TCCGGGAAAA ACTGACGTTTC TATCTGGTTA CCCTTGAGCA
 AGCGCAGGAA CAACAG [SEQ ID NO:73]

10 PMON13064

ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
 15 CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
 AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
 CTGCTCGGAC ACTCTCTGGG CATCCCTGG GCTCCCTGA GCTCCTGCC
 20 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
 TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCCGAG
 25 TTGGGTCCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC
 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTCCA GCGCCGGGCA
 30 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
 CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
 35 CCCCCGGGCC TCCGTCAAT GCTGGCGCG GCTCTGGTGG TGTTCTGGT
 GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG
 CTCTGAGGGT GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTGATT
 40 ATGAAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC
 TAAAGAGAC CACCTAACCC TTGCTGGAC CCGAACAAAC TCAATTCTGA
 45 AGACATGGAT ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG
 CATTGTAAG GGCTGTCAAG CACTTAGAAA ATGCATCAGG TATTGAGGCA
 ATTCTCGTA ATCTCCAACC ATGCTGCCC TCTGCCACGG CGCACCCCTC
 50 TCCACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA TTCCGGGAAA
 AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG
 55 [SEQ ID NO:74]

PMON13043

ATGGCTACAC CATTAGGCCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
 60 CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC

172

AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
 5 CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG GCTCCCCCTGA GCTCCTGCC
 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
 10 TTTTCCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCCGAG
 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC
 15 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTSG AGGTGTCGTA
 CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
 20 CCCCGGGTGG TGGTTCTGGC GGGGGCTCCA ACATGGCTAA CTGCTCTATA
 ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTTGCT
 25 GGACCCGAAC AACCTCAATG AC GAAGACGT CTCTATCCTG ATGGAACGAA
 ACCTTCGACT TCCAAACCTG GAGAGCTTCG TAAGGGCTGT CAAGAACCTA
 GAAAATGCAT CAGGTATTGA GGCAATTCTT CGTAATCTCC AACCATGTCT
 30 GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC ATCAAGGCAG
 GTGACTGGCA AGAATTCCGG GAAAAACTGA CGTTCTATCT GGTTACCCCT
 35 GAGCAAGCGC AGGAACAACA G [SEQ ID NO:75]

PMON13044

40 ATGGCTACAC CATTAGGCCCTGCCAGCTCC CTGCCCCAGA GCTTCCTGCT
 CAAGTGCTTA GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC
 AGGAGAAGCT GTGTGCCACC TACAAGCTGT GCCACCCCGA GGAGCTGGTG
 45 CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG GCTCCCCCTGA GCTCCTGCC
 CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC CATAGCGGCC
 TTTTCCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCCGAG
 50 TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC
 CACCATCTGG CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC
 CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
 55 GGAGGGGTCC TGGTTGCTAG CCATCTGCAG AGCTTCCTGG AGGTGTCGTA
 CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG GGAAGGATTT
 60

173

CCCCCGGGCC TCCTGTCAAT GCTGGCGGGC GCTCTGGTGG TGGTTCTGCT
 5 GCGGGCTCTG AGGCTGGCGG CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG
 CTCTGAGGGT GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTTGATT
 ATGAAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC
 10 TTAAAGAGAC CACCTGCACC TTTGCTGGAC CCGAACAAACC TCAATGACGA
 AGACGTCTCT ATCCTGATGG AACGAAACCT TCGACTTCCA AACCTGGAGA
 GCTTCGTAAG GGCTGTCAAG AACTTAGAAA ATGCATCAGG TATTGAGGCA
 15 ATTCTTCGTA ATCTCCAACC ATGTCTGCC C TCTGCCACGG CCGCACCCCTC
 TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA TTCCGGAAA
 20 AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG
 [SEQ ID NO: 76]

PMON13045

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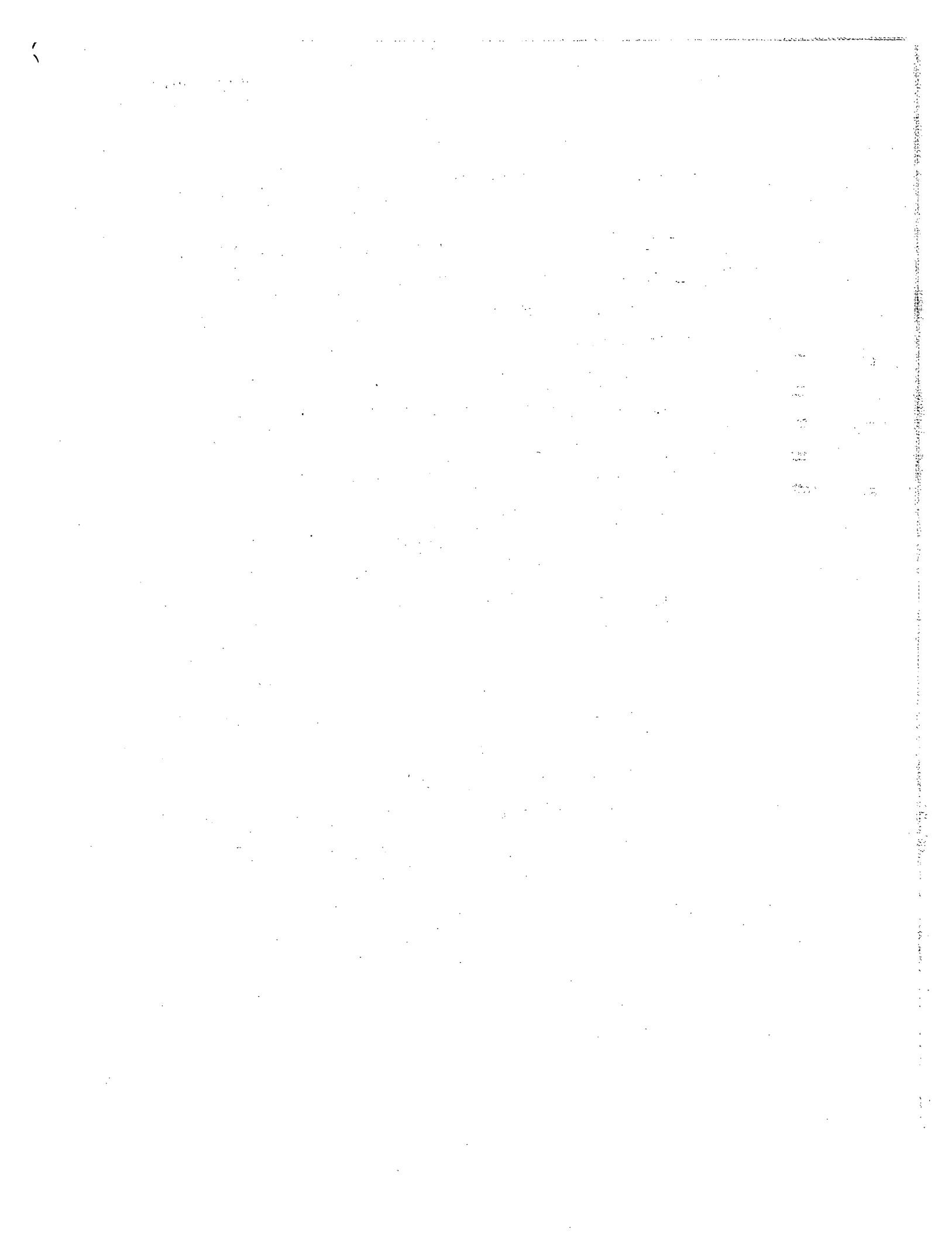
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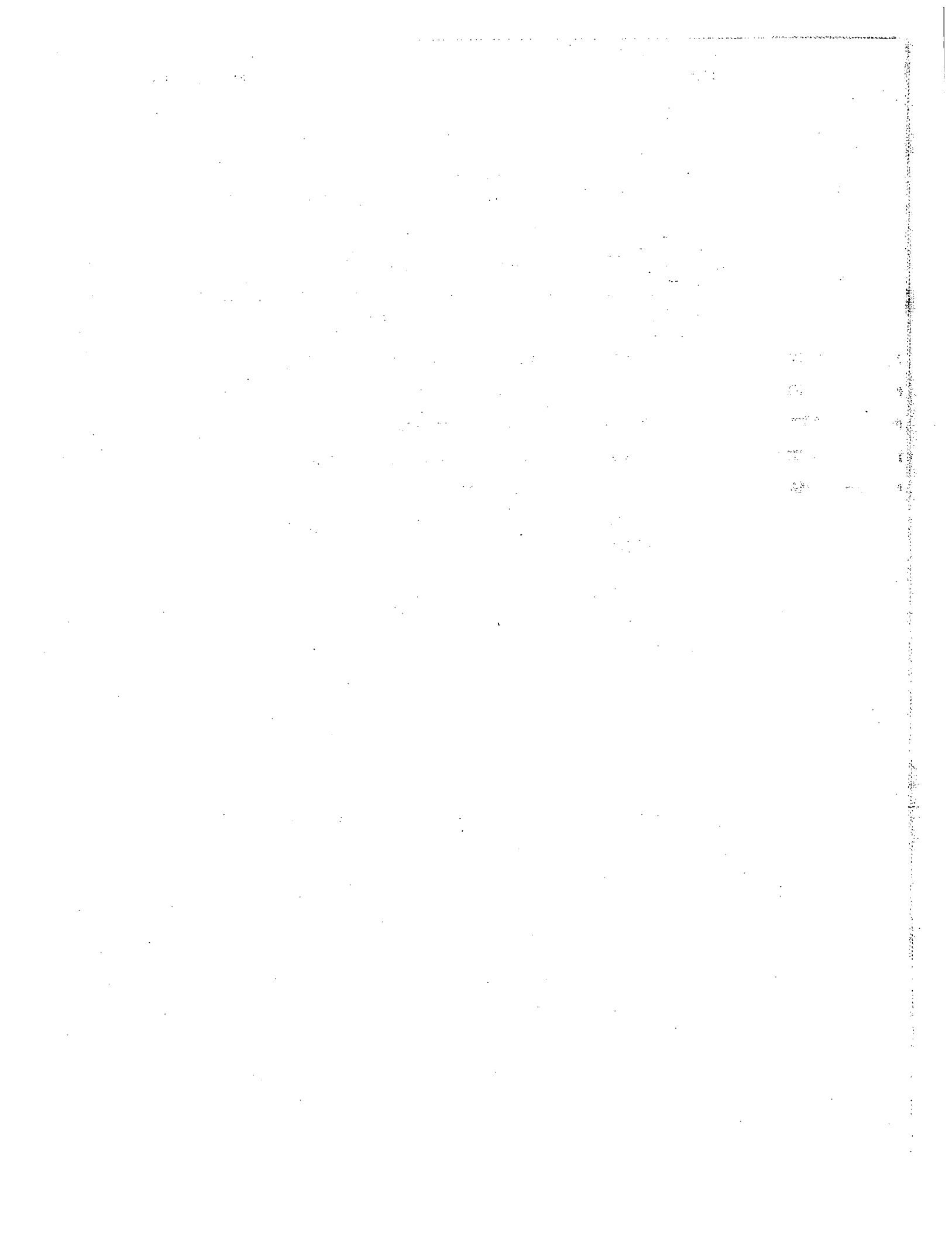
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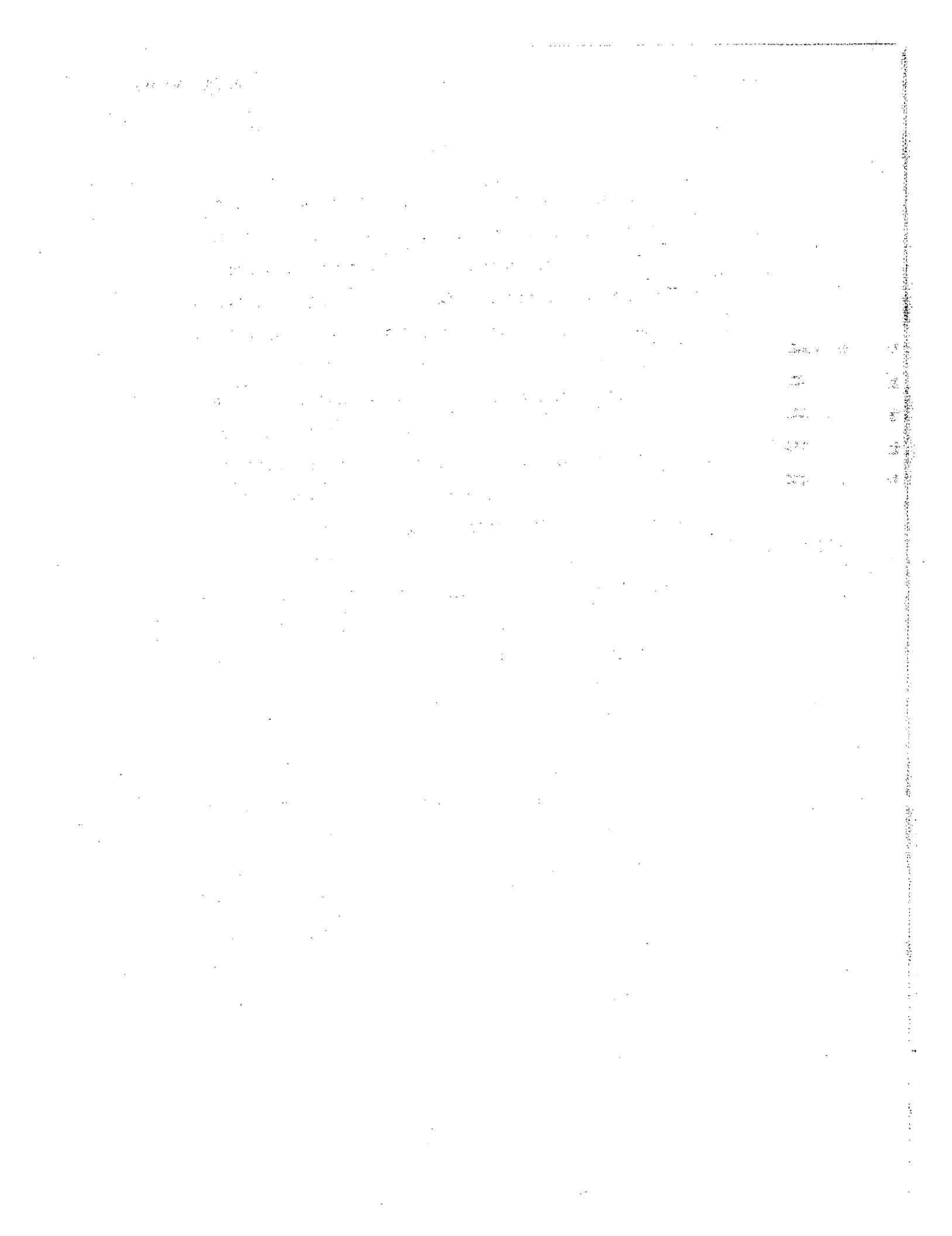
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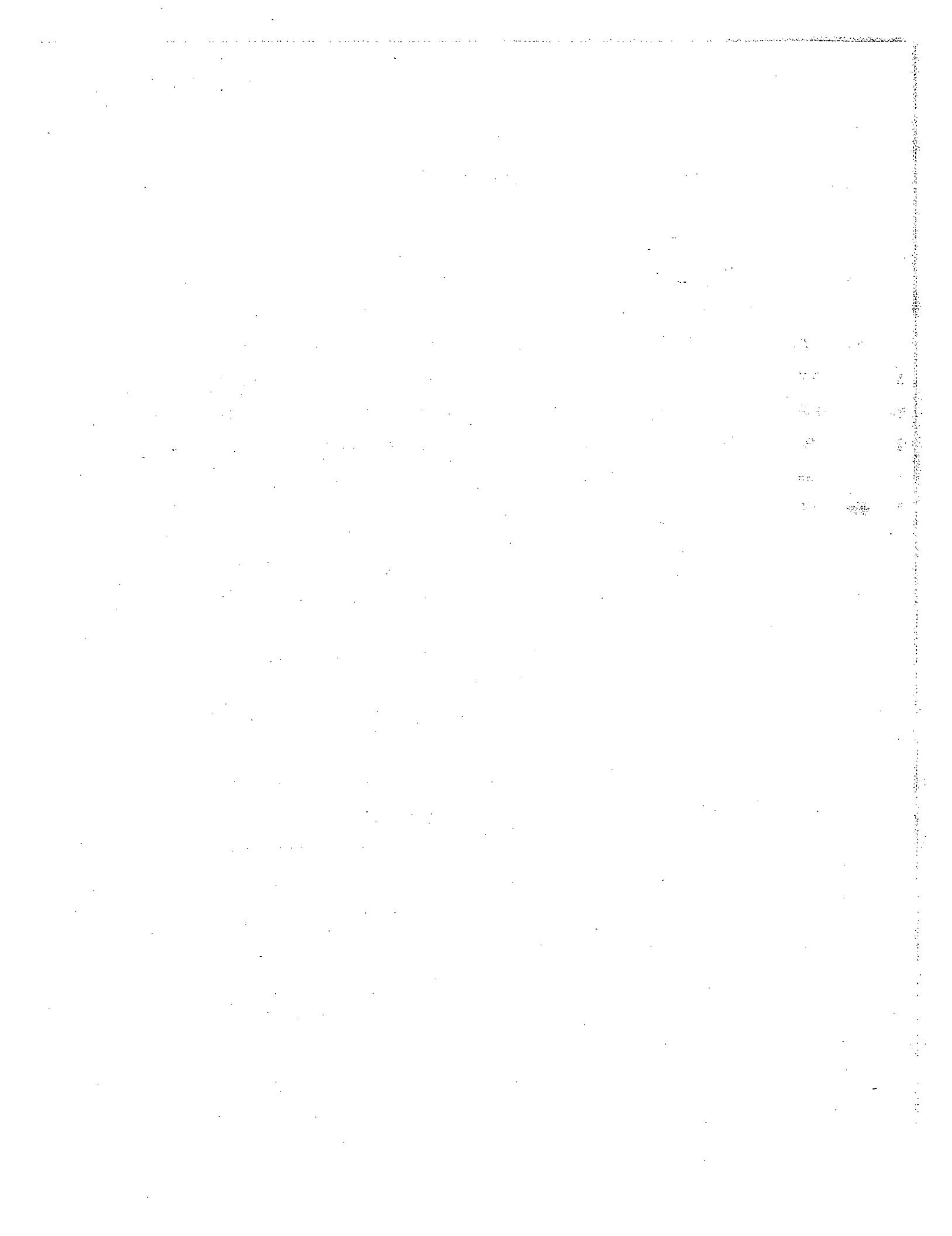


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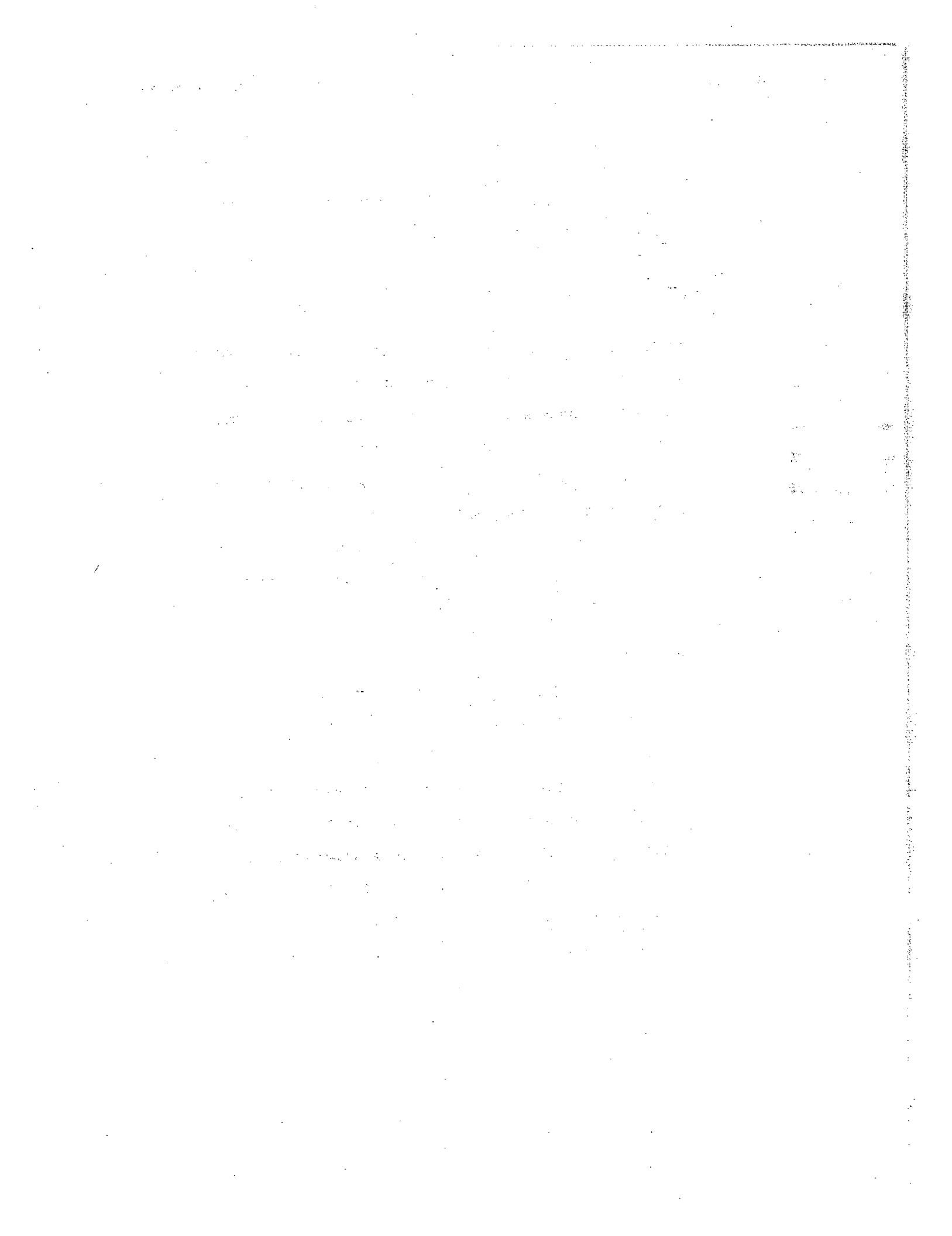
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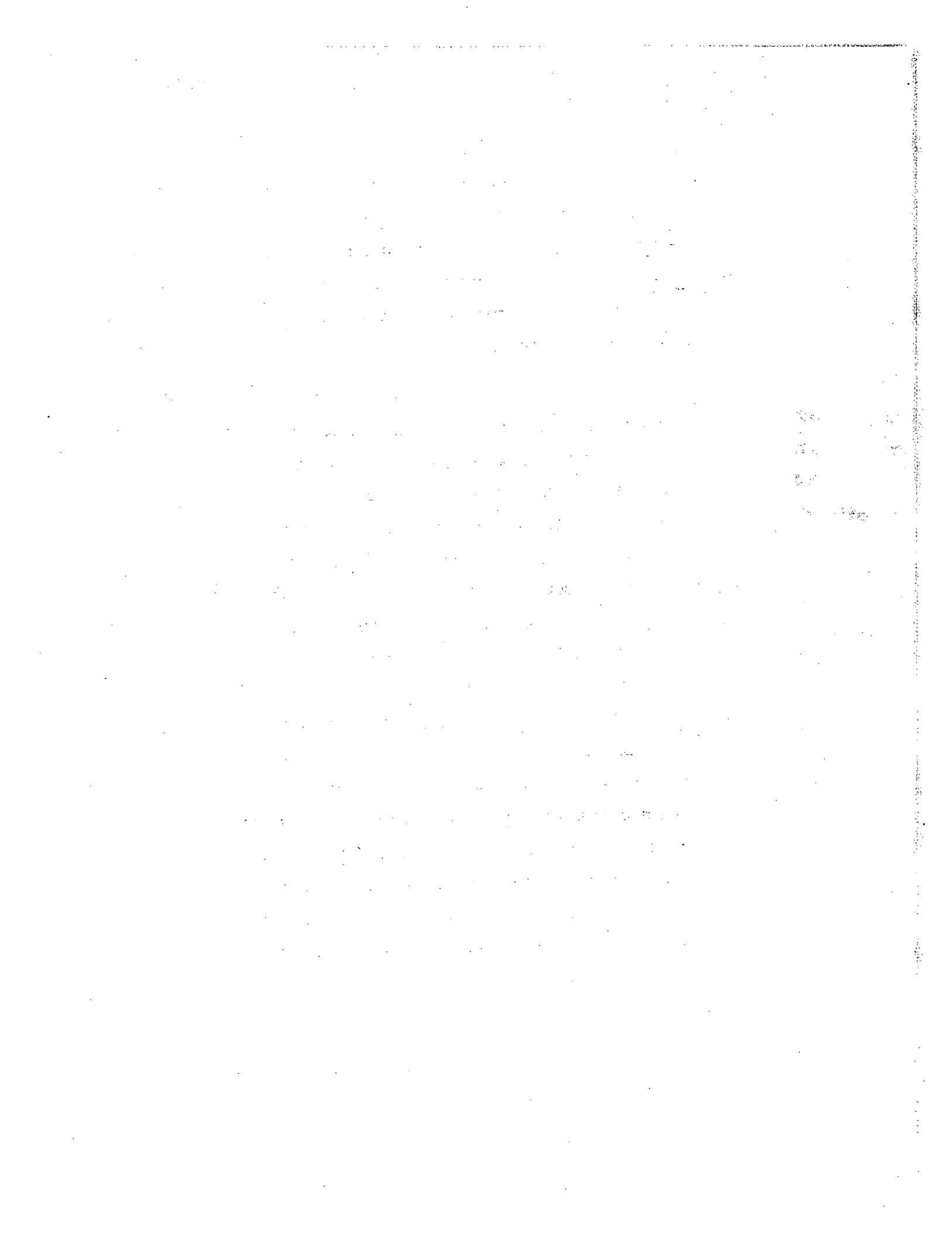
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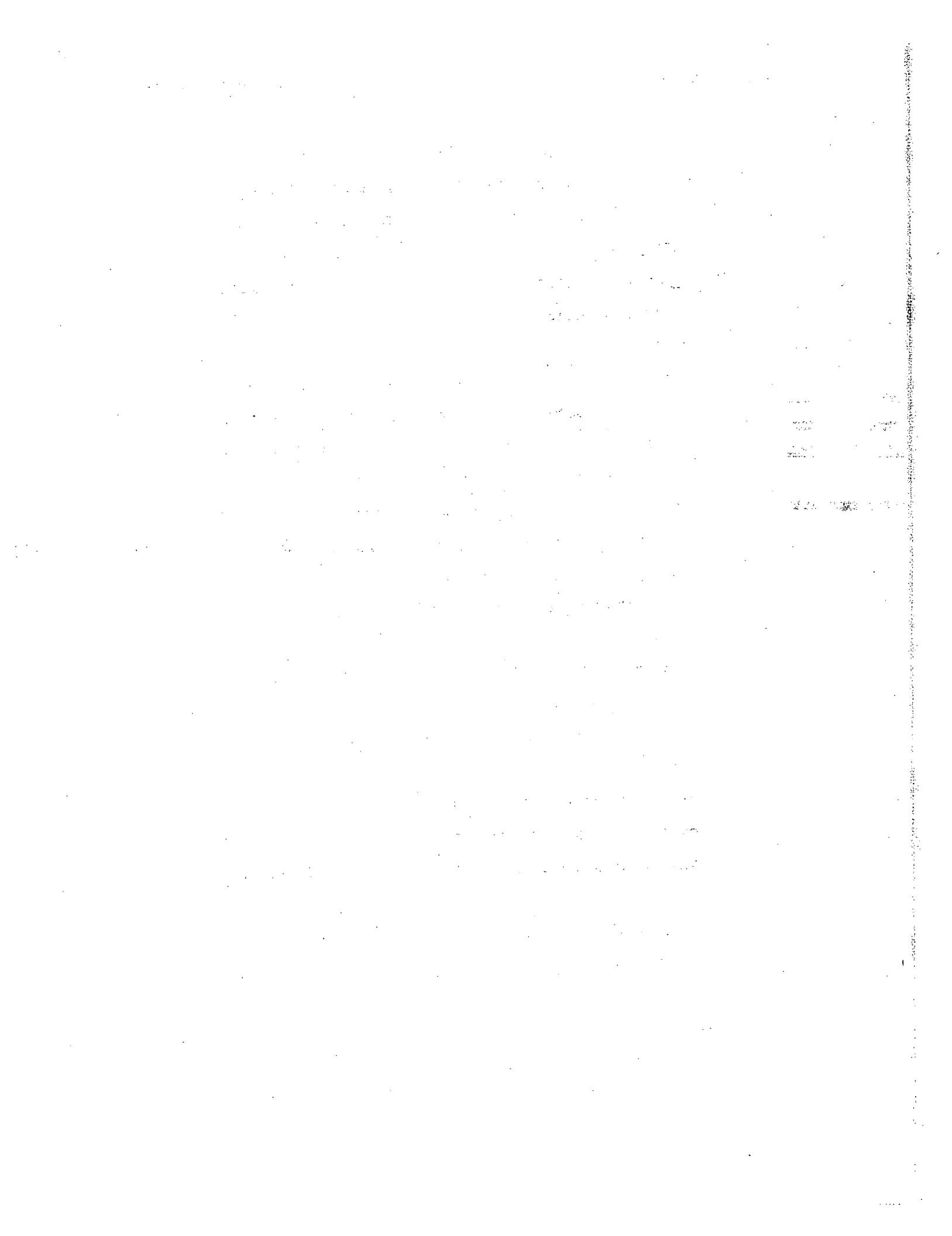
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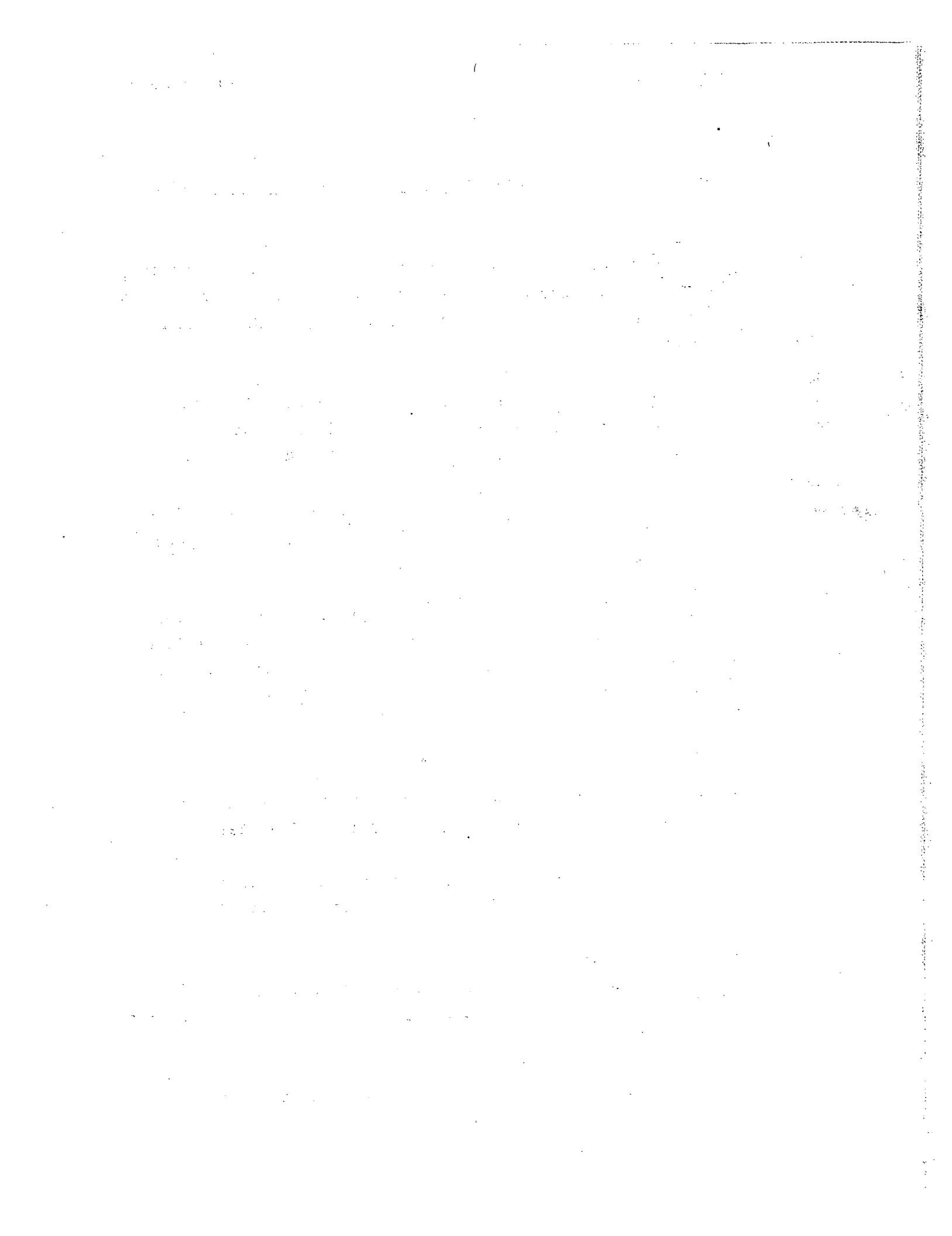
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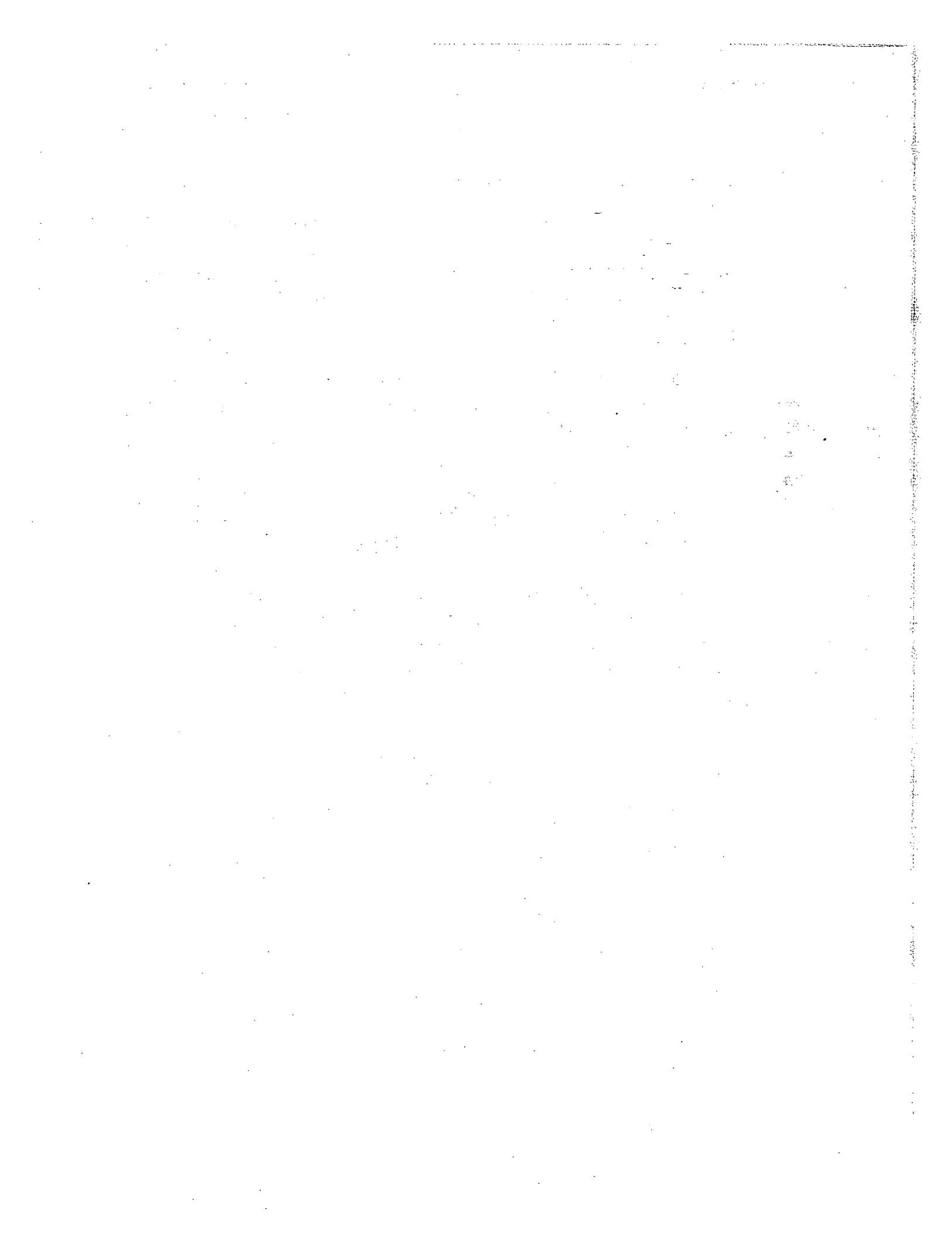
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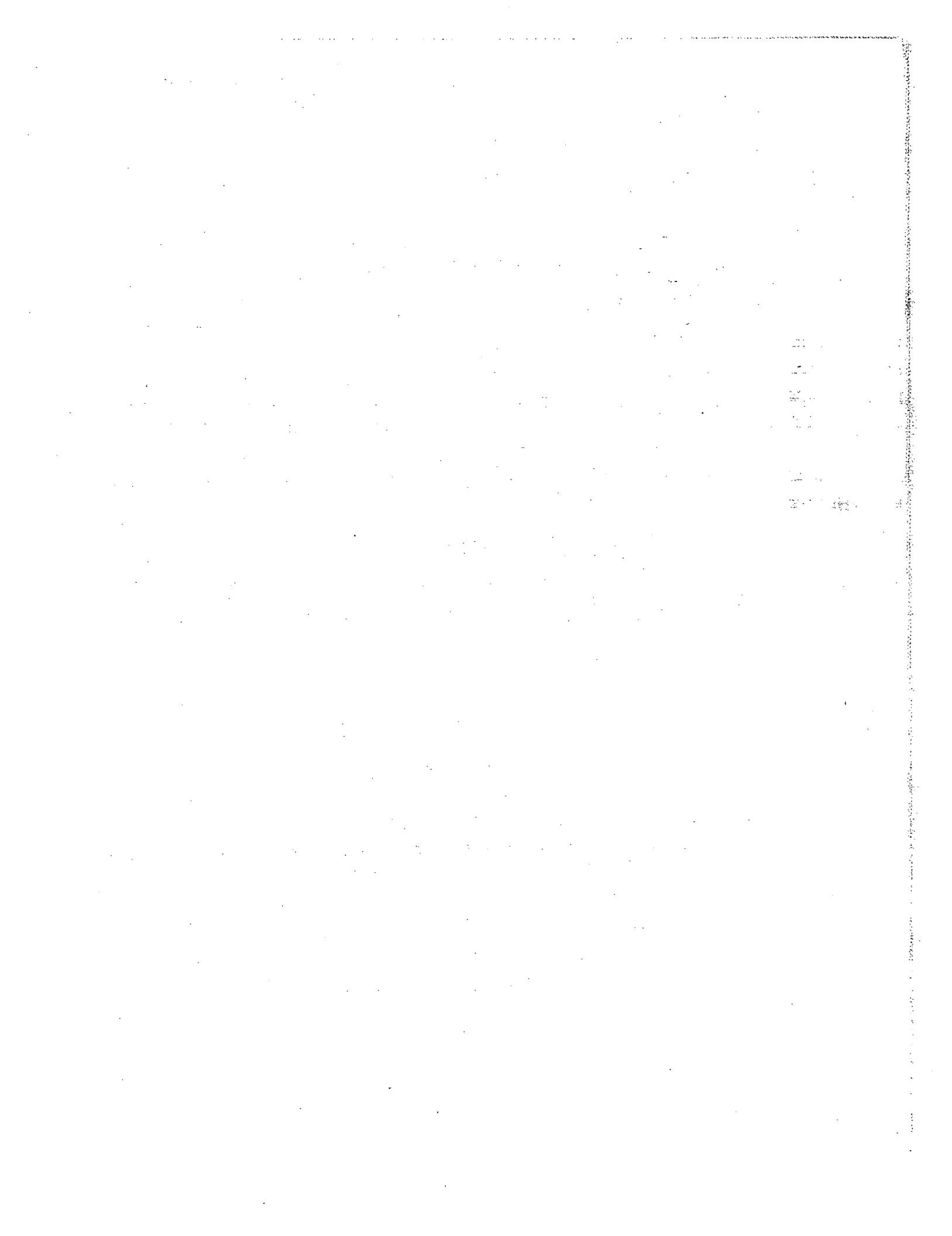
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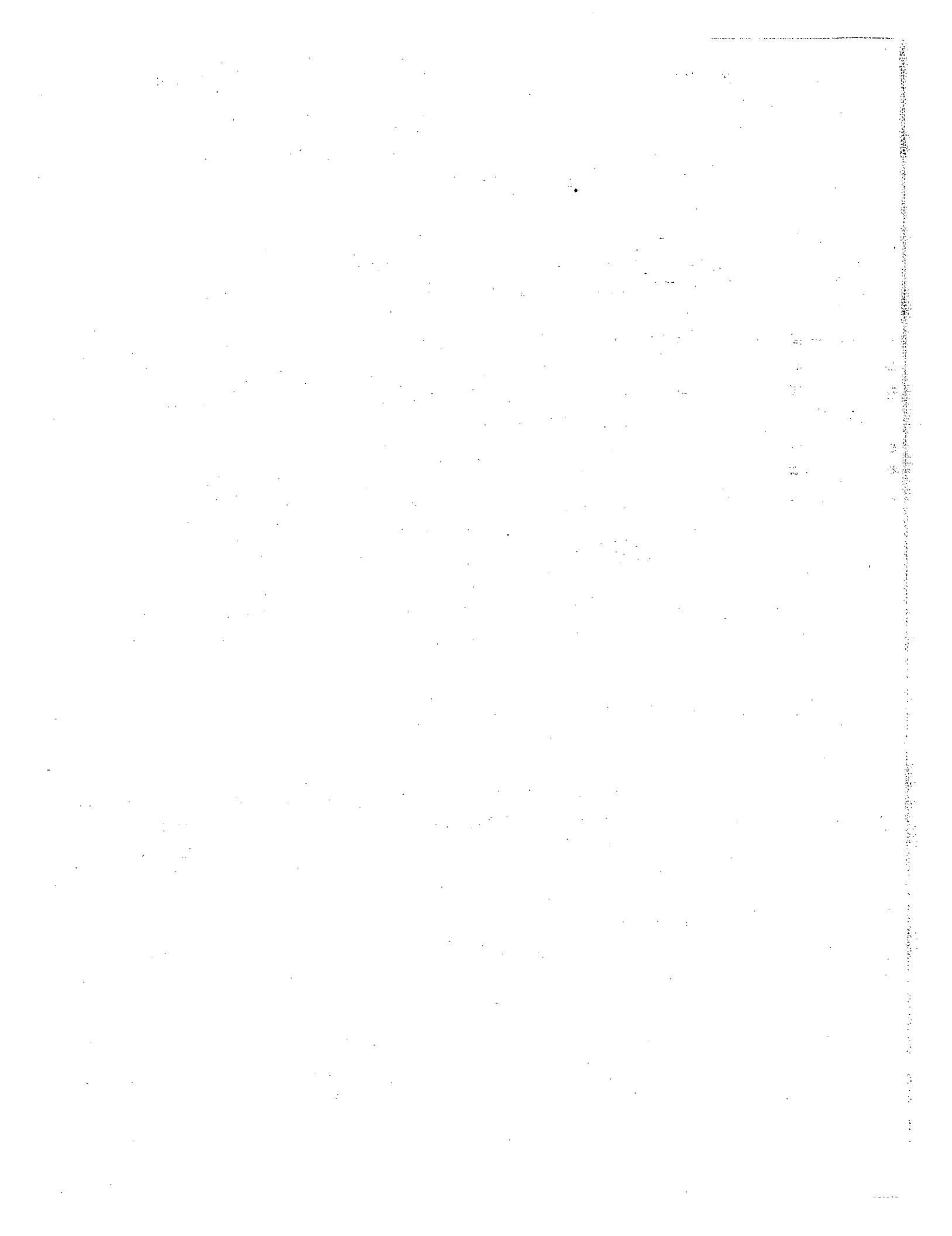
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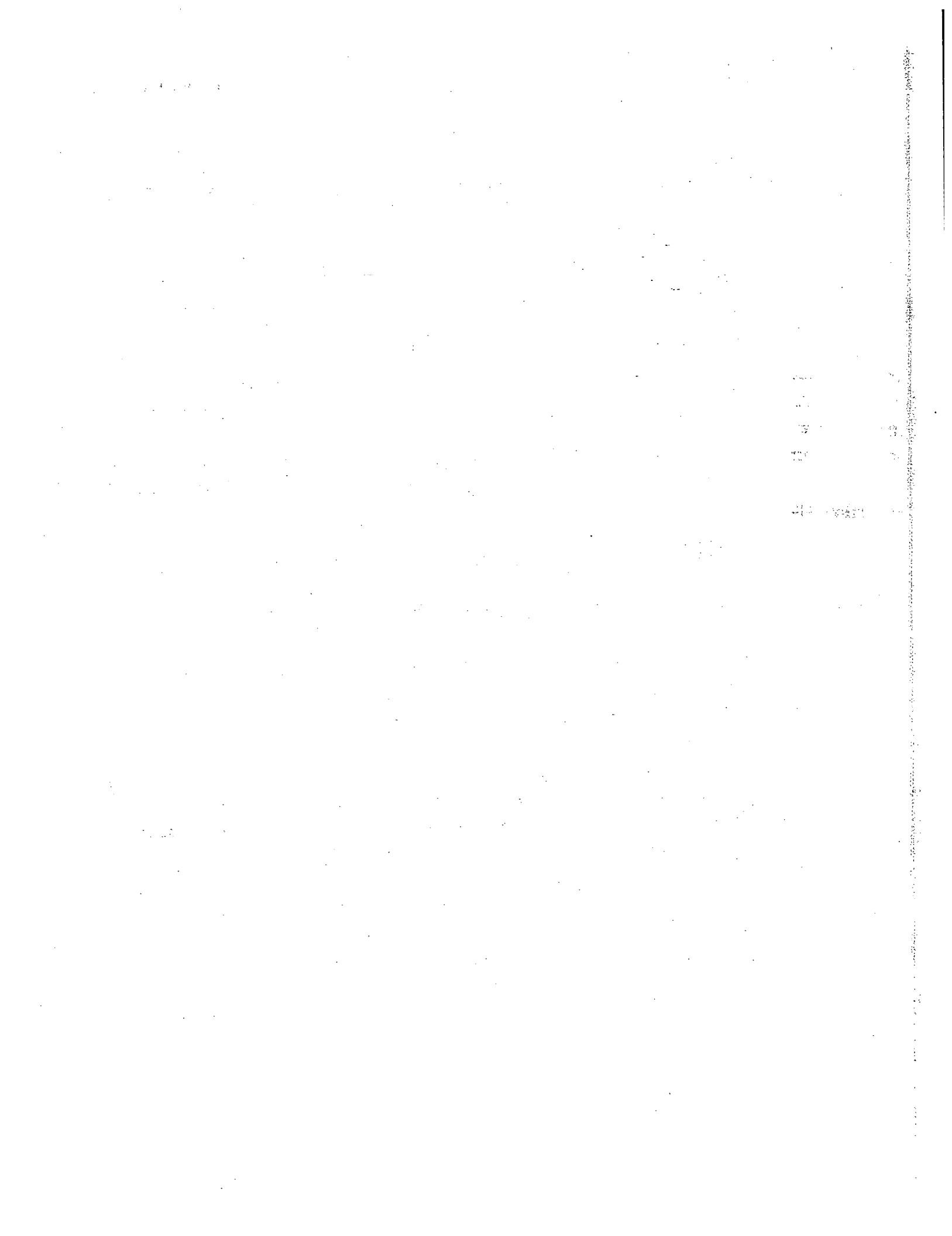
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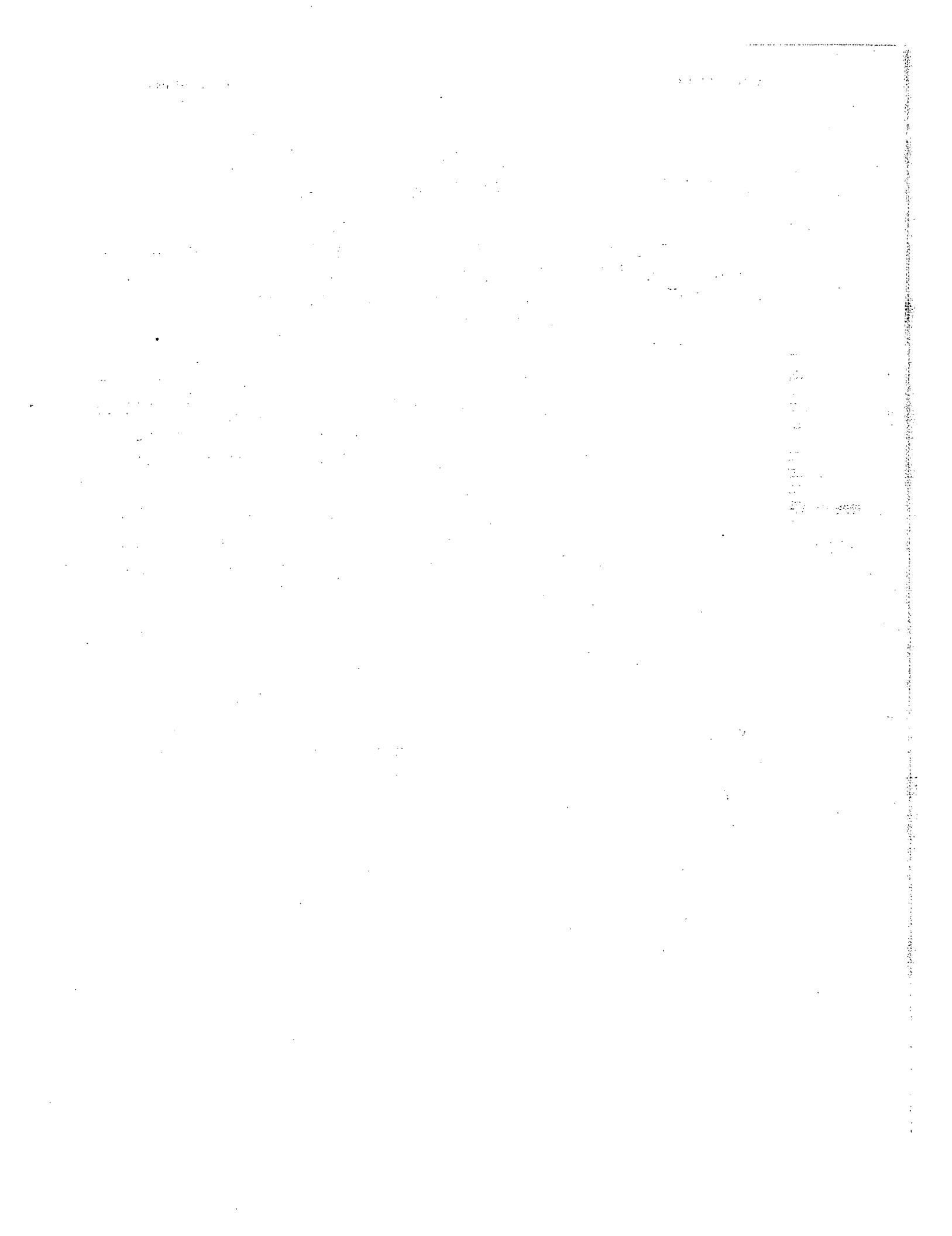
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stranded DNA template. DNA, 3: 479 (1984).

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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 19
- (D) OTHER INFORMATION: /note= "Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /note= "Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, Asn, Thr, Ser, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 22
- (D) OTHER INFORMATION: /note= "Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, Gln, Leu, Val, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /note= "Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys, Phe, Ser, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 24
- (D) OTHER INFORMATION: /note= "Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu"

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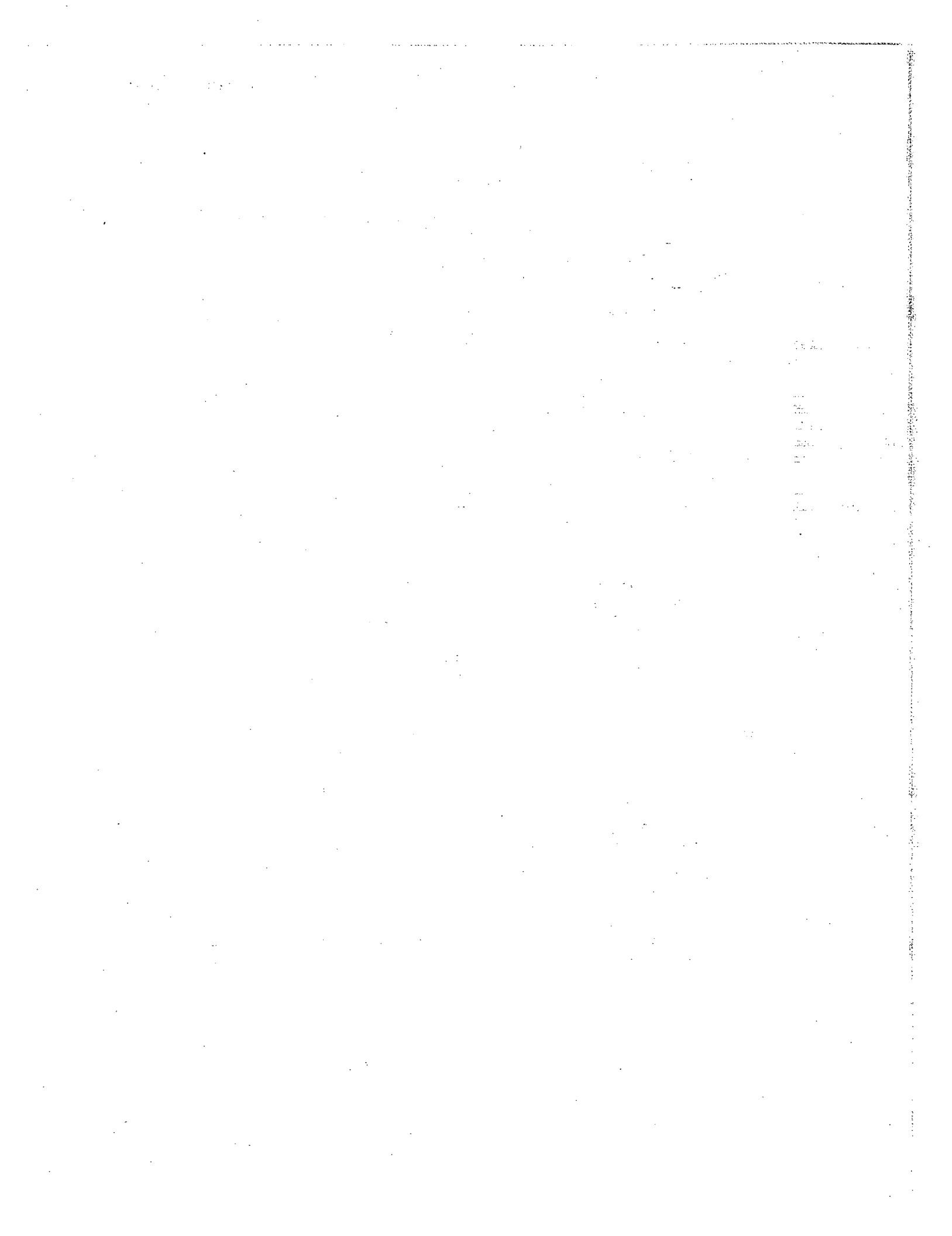
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- (B) LOCATION: 25
- (D) OTHER INFORMATION: /note= "Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 26
- (D) OTHER INFORMATION: /note= "Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 27
- (D) OTHER INFORMATION: /note= "Xaa at position 27 is Leu,"



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Ser, Pro, Trp, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 38
- (D) OTHER INFORMATION: /note= "Xaa at position 38 is Asn, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 40
- (D) OTHER INFORMATION: /note= "Xaa at position 40 is Leu, Trp, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 41
- (D) OTHER INFORMATION: /note= "Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 42
- (D) OTHER INFORMATION: /note= "Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, Val, Glu, Phe, Tyr, Ile, Met, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 43
- (D) OTHER INFORMATION: /note= "Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, Gln, Arg, Thr, Gly, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 44
- (D) OTHER INFORMATION: /note= "Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, Glu, Asn, Gln, Ala, or Pro"

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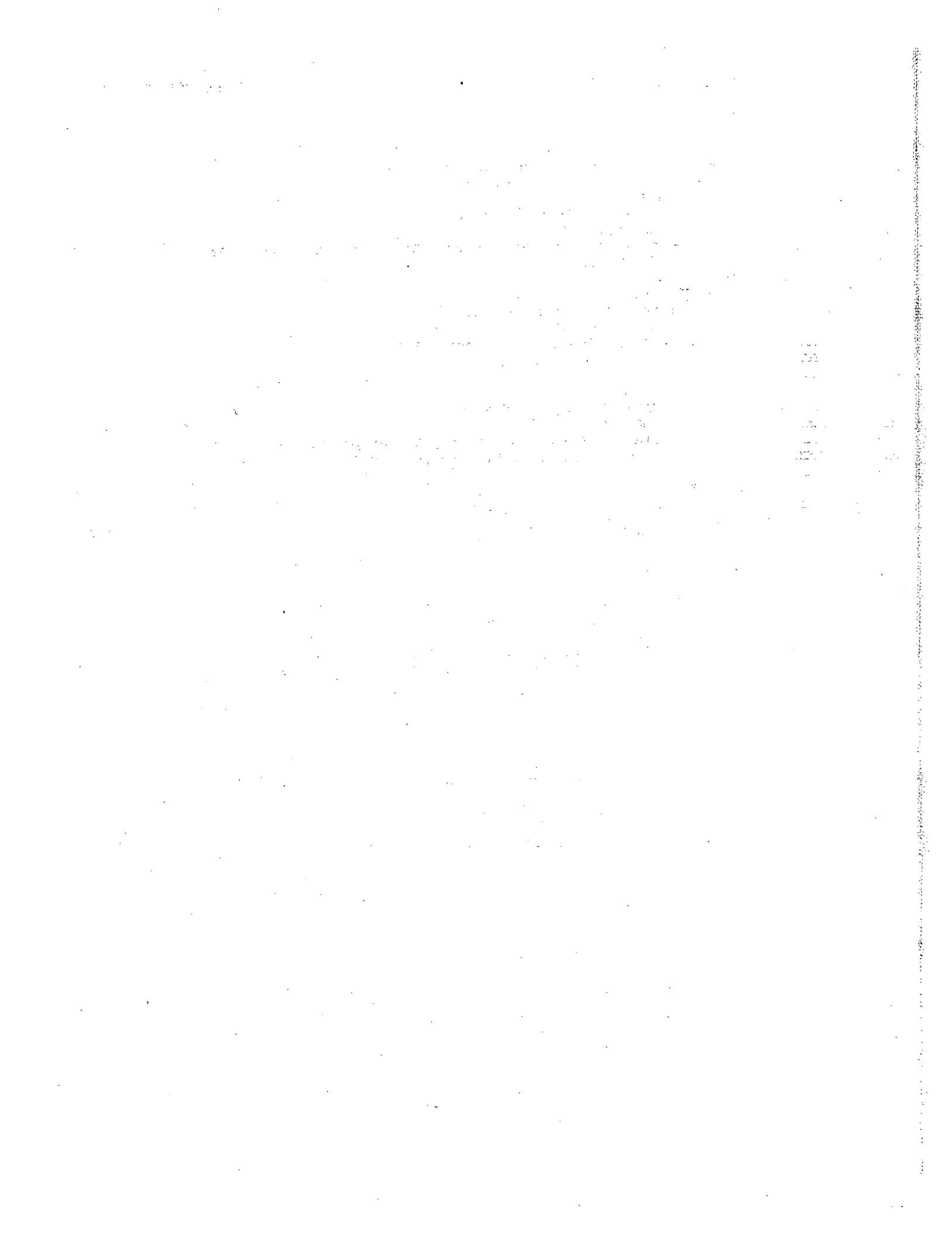
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- (B) LOCATION: 45
- (D) OTHER INFORMATION: /note= "Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, Lys, His, Ala, Tyr, Ile, Val, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 47
- (D) OTHER INFORMATION: /note= "Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His"



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(D) OTHER INFORMATION: /note= "Xaa at position 57 is Asn or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 58

(D) OTHER INFORMATION: /note= "Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 59

(D) OTHER INFORMATION: /note= "Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 60

(D) OTHER INFORMATION: /note= "Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 61

(D) OTHER INFORMATION: /note= "Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 62

(D) OTHER INFORMATION: /note= "Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 63

(D) OTHER INFORMATION: /note= "Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 64

(D) OTHER INFORMATION: /note= "Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 65

(D) OTHER INFORMATION: /note= "Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 66

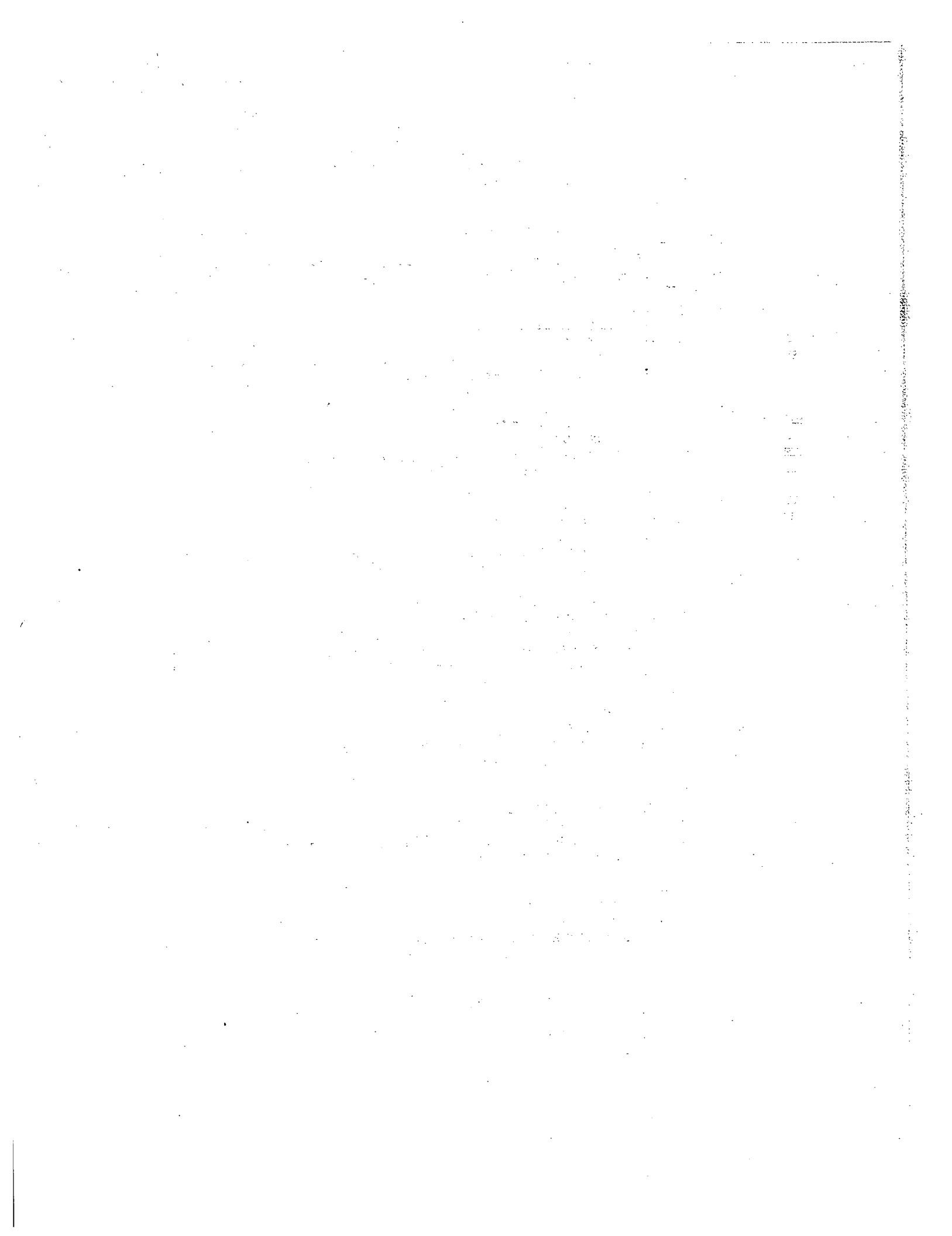
(D) OTHER INFORMATION: /note= "Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 67

(D) OTHER INFORMATION: /note= "Xaa at position 67 is Ser,



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(D) OTHER INFORMATION: /note= "Xaa at position 77 is Ile,
Ser, Arg, Thr, or Leu"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 78

(D) OTHER INFORMATION: /note= "Xaa at position 78 is Leu,
Ala, Ser, Glu, Phe, Gly, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 79

(D) OTHER INFORMATION: /note= "Xaa at position 79 is Lys, Thr,
Asn, Met, Arg, Ile, Gly, or Asp"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 80

(D) OTHER INFORMATION: /note= "Xaa at position 80 is Asn,
Trp, Val, Gly, Thr, Leu, Glu, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 81

(D) OTHER INFORMATION: /note= "Xaa at position 81 is Leu,
Gln, Gly, Ala, Trp, Arg, Val, or Lys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 82

(D) OTHER INFORMATION: /note= "Xaa at position 82 is Leu,
Gln, Lys, Trp, Arg, Asp, Glu, Asn, His, Thr, Ser, Ala,
Tyr, Phe, Ile, Met, or Val"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 83

(D) OTHER INFORMATION: /note= "Xaa at position 83 is Pro,
Ala, Thr, Trp, Arg, or Met"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 84

(D) OTHER INFORMATION: /note= "Xaa at position 84 is Cys,
Glu, Gly, Arg, Met, or Val"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 85

(D) OTHER INFORMATION: /note= "Xaa at position 85 is Leu,
Asn, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

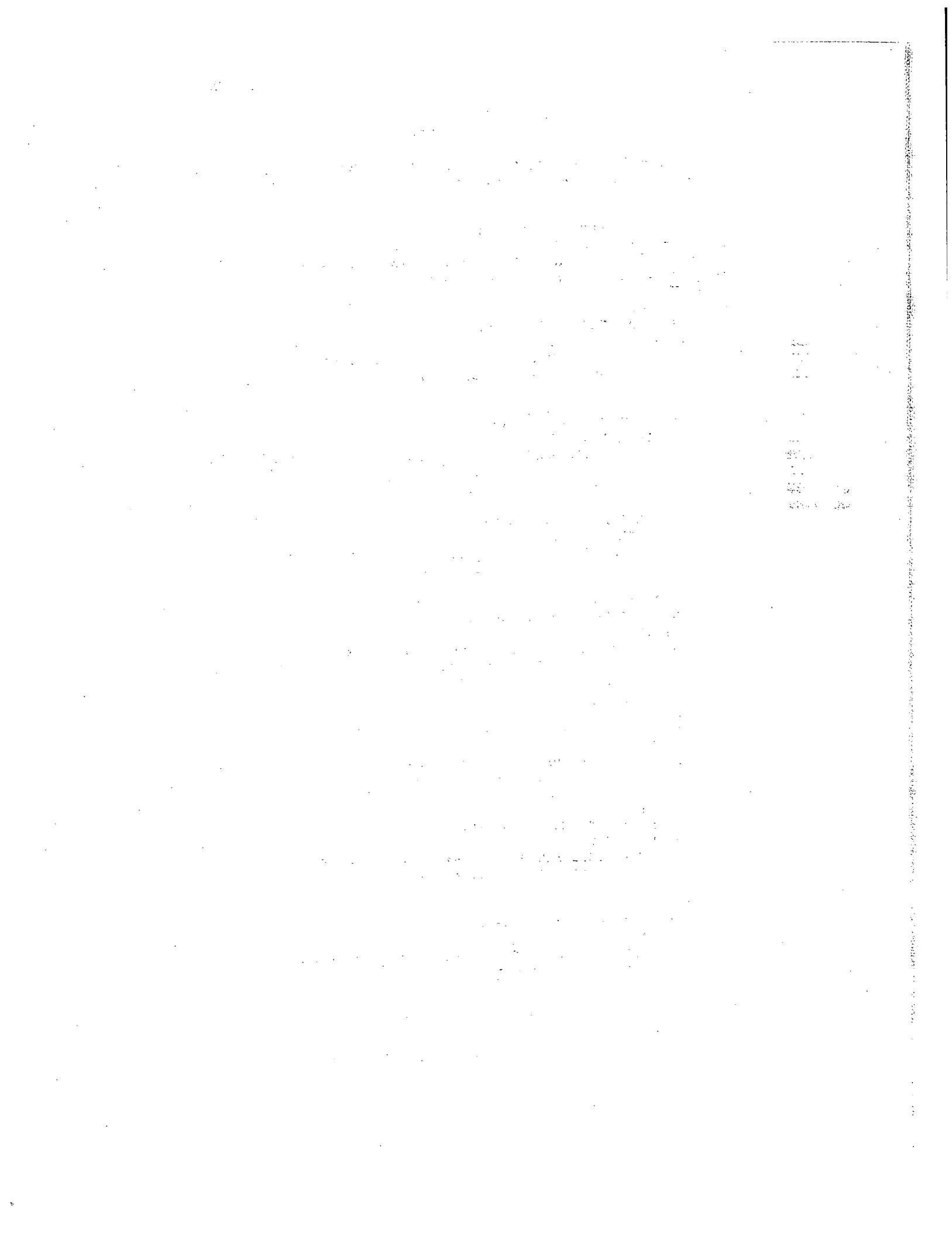
(B) LOCATION: 86

(D) OTHER INFORMATION: /note= "Xaa at position 86 is Pro,
Cys, Arg, Ala, or Lys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 87



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(D) OTHER INFORMATION: /note= "Xaa at position 97 is Ile,
Val, Lys, Ala, or Asn"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 98

(D) OTHER INFORMATION: /note= "Xaa at position 98 is His,
Ile, Asn, Leu, Asp, Ala, Thr, Glu, Gln, Ser, Phe, Met,
Val, Lys, Arg, Tyr, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 99

(D) OTHER INFORMATION: /note= "Xaa at position 99 is Ile,
Leu, Arg, Asp, Val, Pro, Gln, Gly, Ser, Phe,
or His"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 100

(D) OTHER INFORMATION: /note= "Xaa at position 100 is
Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 101

(D) OTHER INFORMATION: /note= "Xaa at position 101 is
Asp, Pro, Met, Lys, His, Thr, Val, Tyr, Glu, Asn, Ser,
Ala, Gly, Ile, Leu, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 102

(D) OTHER INFORMATION: /note= "Xaa at position 102 is Gly,
Leu, Glu, Lys, Ser, Tyr, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 103

(D) OTHER INFORMATION: /note= "Xaa at position 103 is Asp,
or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 104

(D) OTHER INFORMATION: /note= "Xaa at position 104 is
Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, Gln, Lys, Ala,
Phe, or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 105

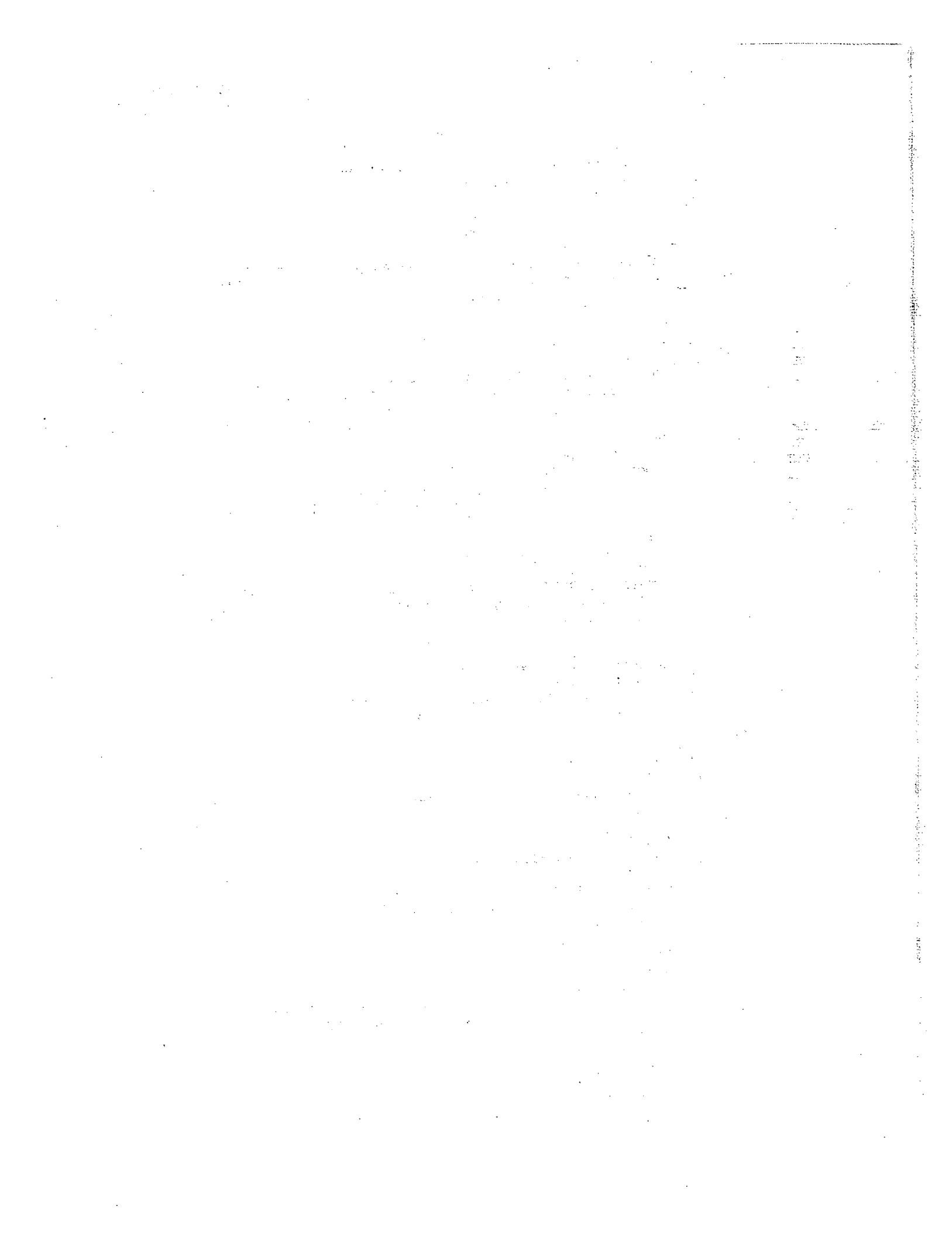
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Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, Leu, Lys, Ile,
Asp, or His"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 106

(D) OTHER INFORMATION: /note= "Xaa at position 106 is Glu,
Ser, Ala, Lys, Thr, Ile, Gly, or Pro"



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(D) OTHER INFORMATION: /note= "Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 118
 (D) OTHER INFORMATION: /note= "Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 119
 (D) OTHER INFORMATION: /note= "Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 120
 (D) OTHER INFORMATION: /note= "Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 121
 (D) OTHER INFORMATION: /note= "Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 122
 (D) OTHER INFORMATION: /note= "Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
 (B) LOCATION: 123
 (D) OTHER INFORMATION: /note= "Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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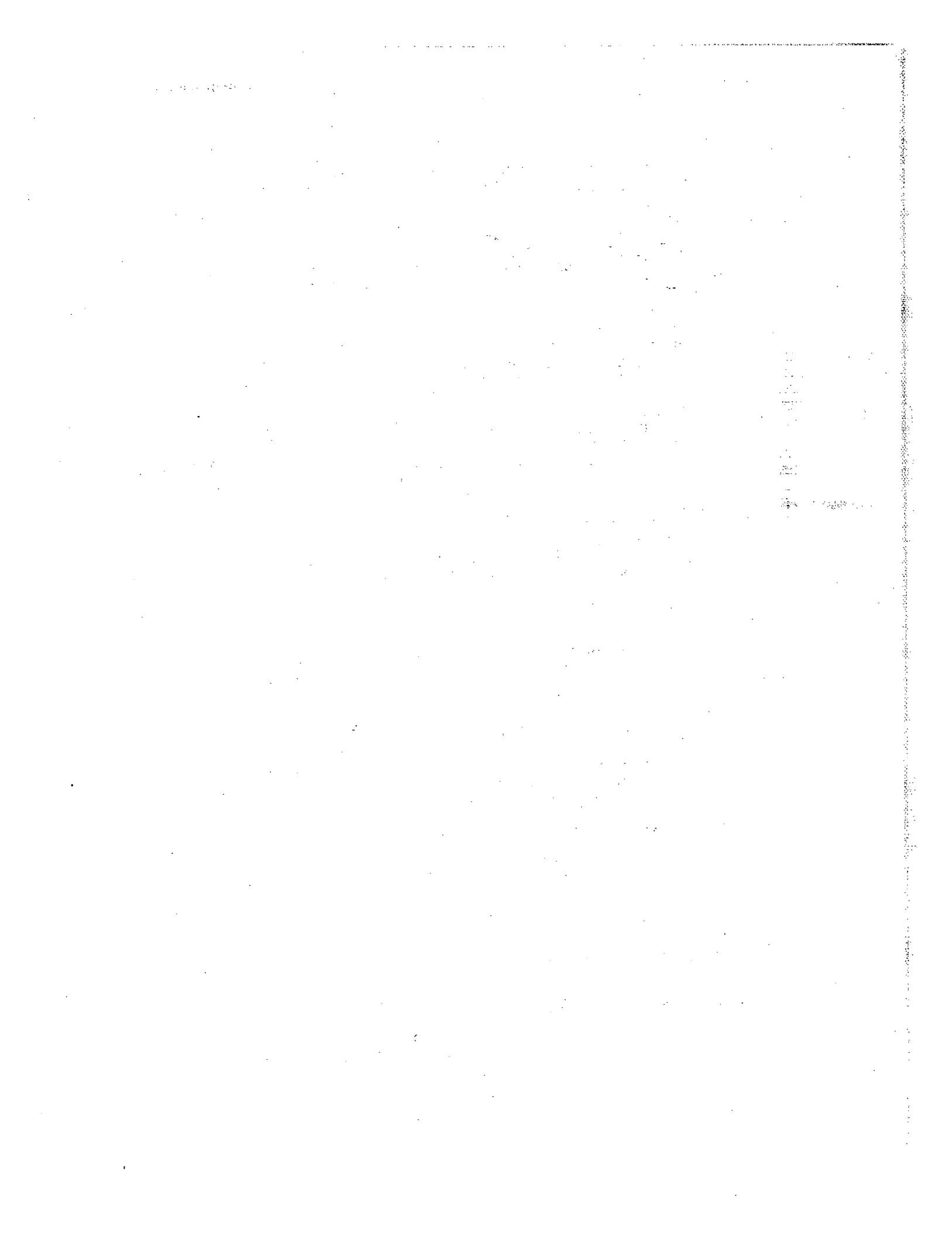
Xaa															
				20				25					30		

Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Asn	Xaa								
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Xaa															
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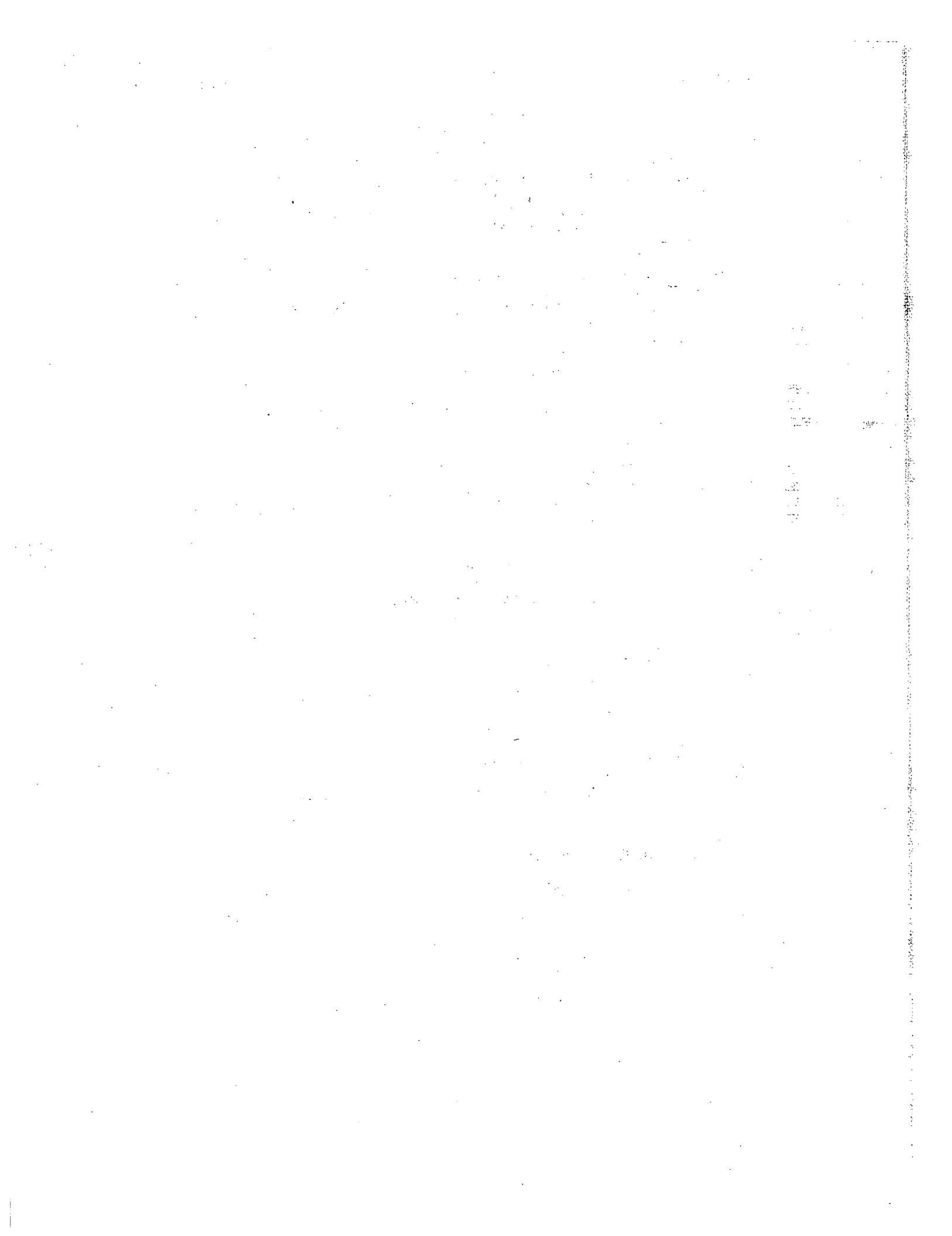
Xaa															
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Xaa															
				85		90					95				



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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 25
 - (D) OTHER INFORMATION: /note= "Xaa at position 25 is Thr, His, Gln, or Ala"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 26
 - (D) OTHER INFORMATION: /note= "Xaa at position 26 is His or Ala"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 29
 - (D) OTHER INFORMATION: /note= "Xaa at position 29 is Gln, Asn, or Val"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 30
 - (D) OTHER INFORMATION: /note= "Xaa at position 30 is Pro, Gly, or Gln"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 31
 - (D) OTHER INFORMATION: /note= "Xaa at position 31 is Pro, Asp, Gly, or Gln"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 32
 - (D) OTHER INFORMATION: /note= "Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or Glu"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 33
 - (D) OTHER INFORMATION: /note= "Xaa at position 33 is Pro or Glu"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 34
 - (D) OTHER INFORMATION: /note= "Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 35
 - (D) OTHER INFORMATION: /note= "Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 37
 - (D) OTHER INFORMATION: /note= "Xaa at position 37 is Phe, Ser, Pro, or Trp"
- (ix) FEATURE:



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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 60
- (D) OTHER INFORMATION: /note= "Xaa at position 60 is Ala or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 62
- (D) OTHER INFORMATION: /note= "Xaa at position 62 is Asn, Pro, Thr, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 63
- (D) OTHER INFORMATION: /note= "Xaa at position 63 is Arg or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 64
- (D) OTHER INFORMATION: /note= "Xaa at position 64 is Ala or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Val or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 66
- (D) OTHER INFORMATION: /note= "Xaa at position 66 is Lys or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 67
- (D) OTHER INFORMATION: /note= "Xaa at position 67 is Ser Phe or His"

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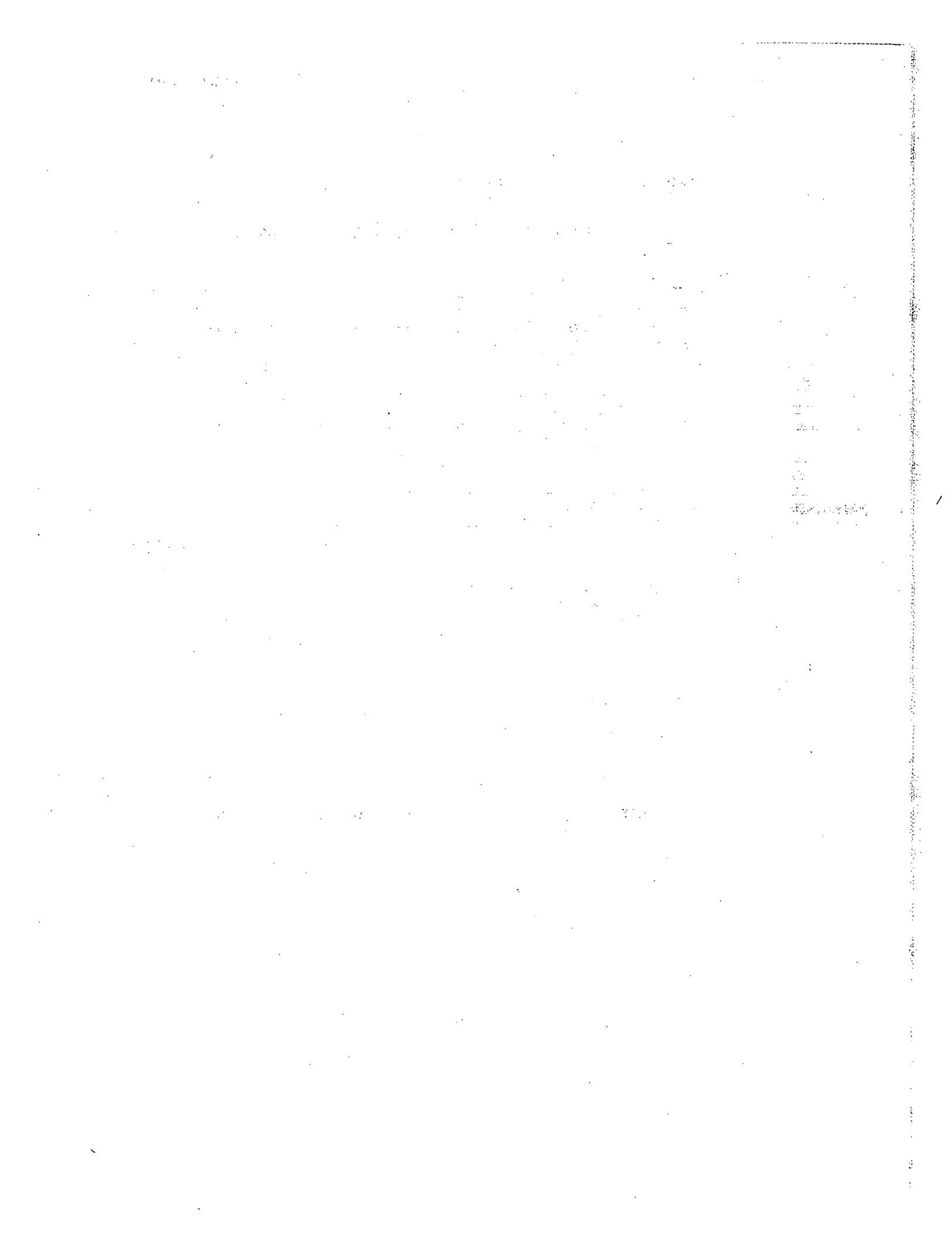
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68
- (D) OTHER INFORMATION: /note= "Xaa at position 68 is Leu, Ile, Phe, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 69
- (D) OTHER INFORMATION: /note= "Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 71
- (D) OTHER INFORMATION: /note= "Xaa at position 71 is Ala, Pro, or Arg"



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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 88
- (D) OTHER INFORMATION: /note= "Xaa at position 88 is Ala or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 91
- (D) OTHER INFORMATION: /note= "Xaa at position 91 is Ala or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 93
- (D) OTHER INFORMATION: /note= "Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn, Phe, Ser, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 96
- (D) OTHER INFORMATION: /note= "Xaa at position 96 is Pro or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 97
- (D) OTHER INFORMATION: /note= "Xaa at position 97 is Ile or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Arg, Gln, Lys, Met, Ser, Tyr, Val, or Pro"

(ix) FEATURE:

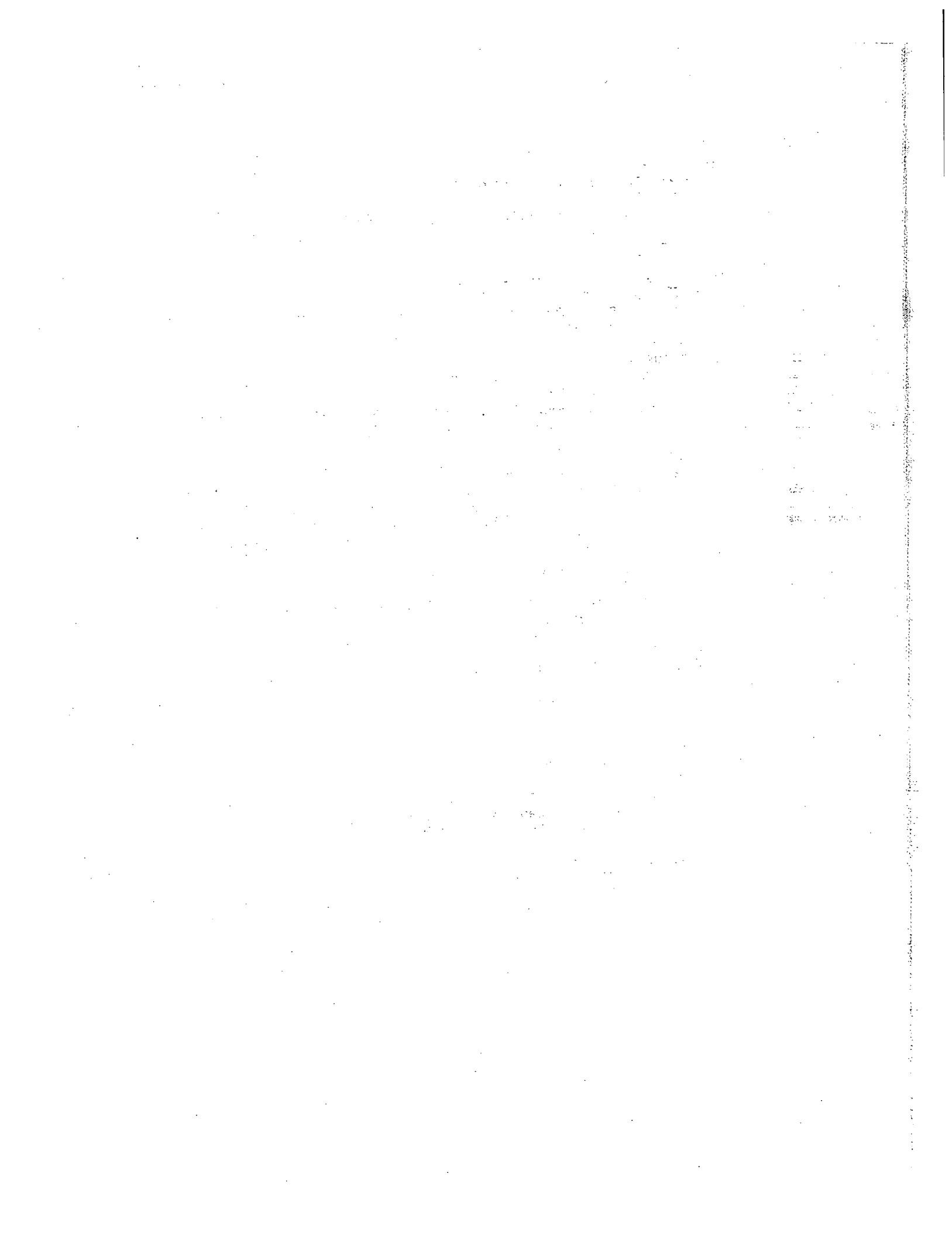
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 99
- (D) OTHER INFORMATION: /note= "Xaa at position 99 is Ile, Leu, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Asn, Ile, Leu, or Tyr"



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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 120
- (D) OTHER INFORMATION: /note= "Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 121
- (D) OTHER INFORMATION: /note= "Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 122
- (D) OTHER INFORMATION: /note= "Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 123
- (D) OTHER INFORMATION: /note= "Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ala	Pro	Met	Thr	Gln	Thr	Thr	Ser	Leu	Lys	Thr	Ser	Trp	Val	Asn	Cys
1				5				10					15		

Xaa	Xaa	Xaa	Ile	Xaa	Glu	Xaa	Xaa	Xaa	Leu	Lys	Xaa	Xaa	Xaa	Xaa	
			20				25				30				

Xaa	Xaa	Xaa	Asp	Xaa	Xaa	Asn	Leu	Asn	Xaa	Glu	Xaa	Xaa	Ile	Leu	
			35			40					45				

Met	Xaa	Xaa	Asn	Leu	Xaa	Xaa	Xaa	Asn	Leu	Glu	Xaa	Phe	Xaa	Xaa	Xaa
			50			55			60						

Xaa	Xaa	Xaa	Xaa	Xaa	Asn	Xaa	Xaa	Ile	Glu	Xaa	Xaa	Leu	Xaa	Xaa	
			65		70			75			80				

Leu	Xaa	Xaa	Cys	Xaa	Pro	Xaa	Xaa	Thr	Ala	Xaa	Pro	Xaa	Arg	Xaa	Xaa
			85				90					95			

Xaa	Xaa	Xaa	Xaa	Xaa	Gly	Asp	Xaa	Xaa	Phe	Xaa	Xaa	Lys	Leu	Xaa	
			100			105					110				

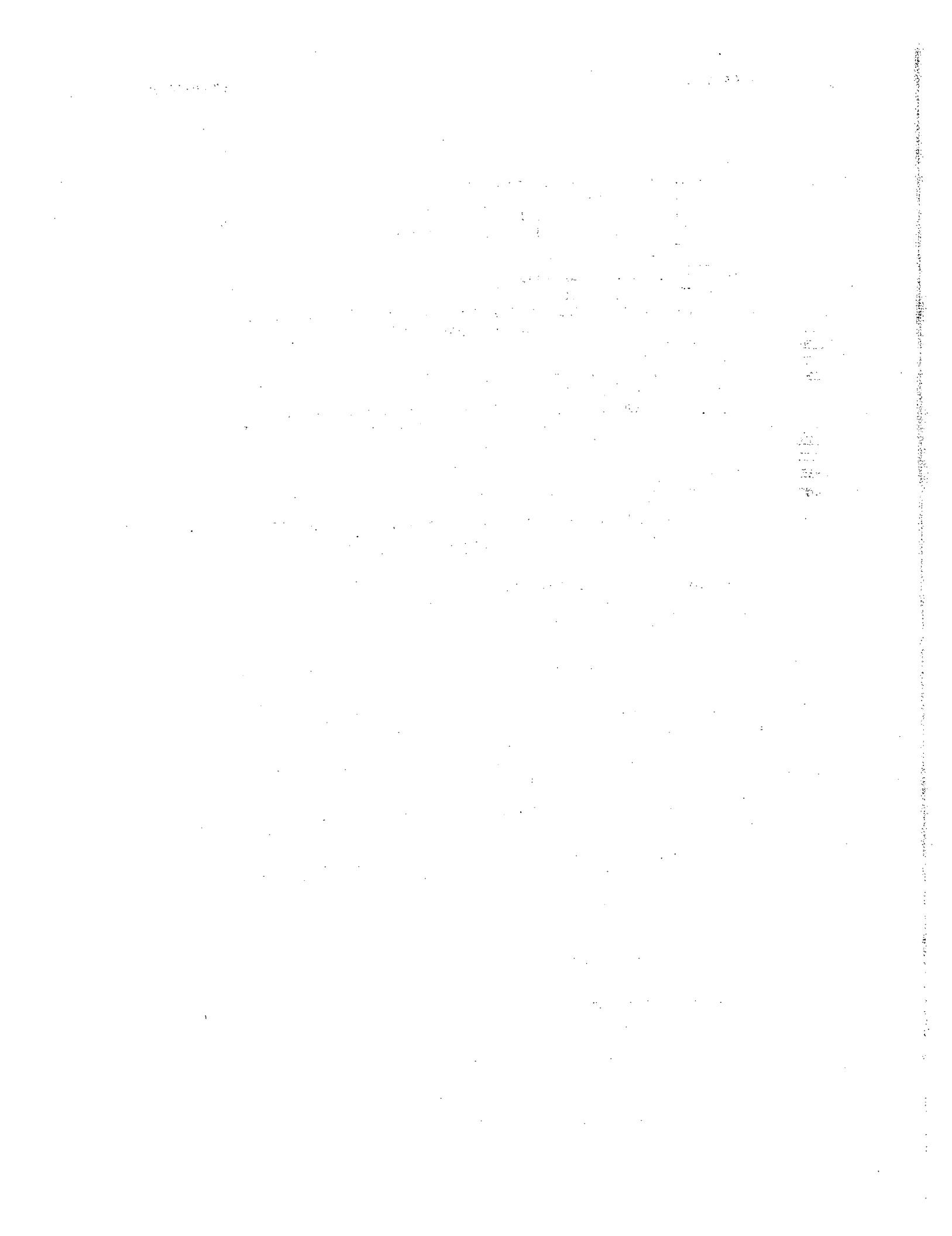
Phe	Xaa	Xaa	Xaa	Xaa	Leu	Glu	Xaa	Xaa	Xaa	Gln	Gln	Thr	Thr	Leu	
			115			120				125					

Ser	Leu	Ala	Ile	Phe											
			130												

(2) INFORMATION FOR SEQ ID NO:3:

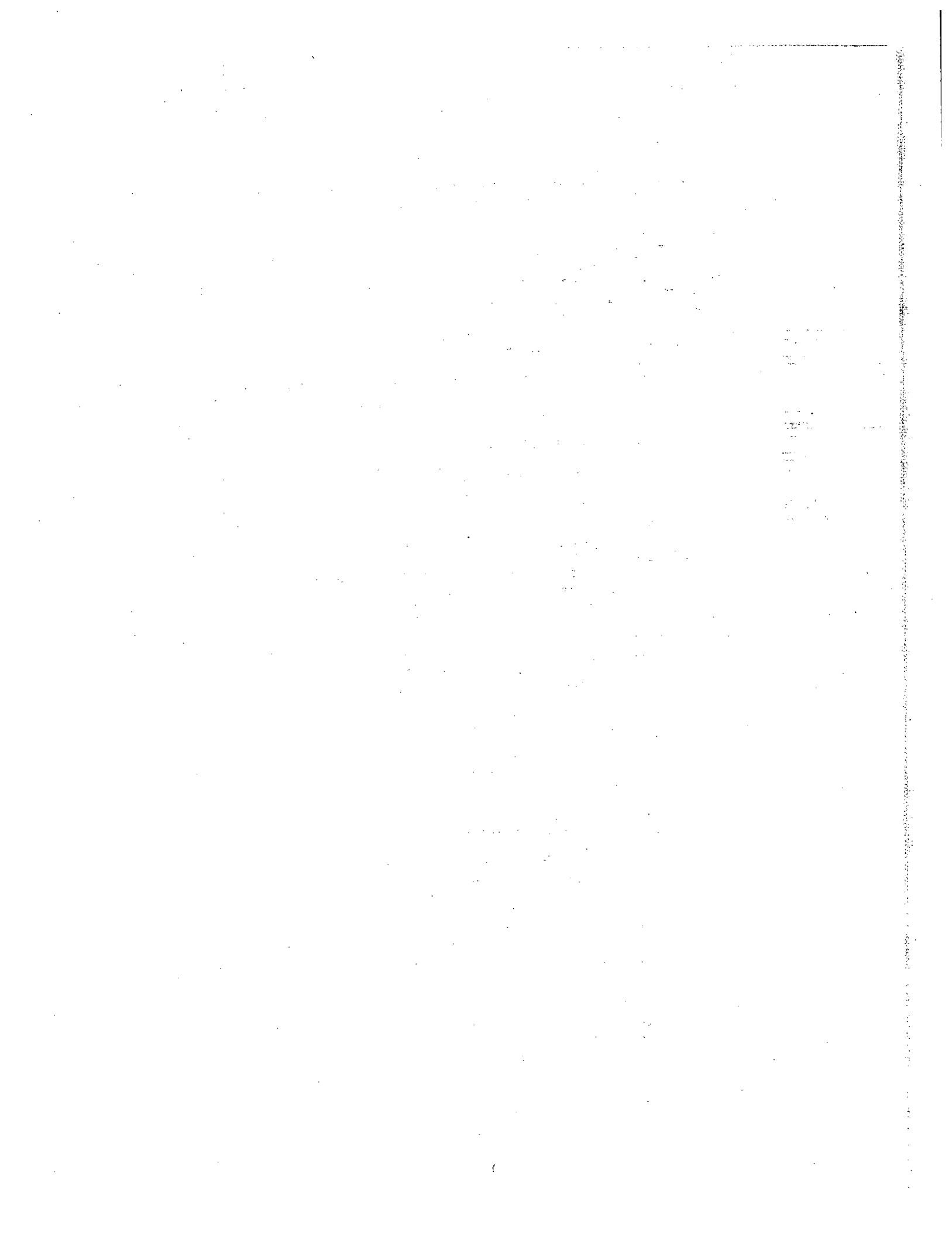
(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 133 amino acids
- (B) TYPE: amino acid



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- (B) LOCATION: 34
(D) OTHER INFORMATION: /note= "Xaa at position 34 is Leu,
Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 35
(D) OTHER INFORMATION: /note= "Xaa at position 35 is Leu,
Ala, Asn, or Pro"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 38
(D) OTHER INFORMATION: /note= "Xaa at position 38 is Asn
or Ala"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 42
(D) OTHER INFORMATION: /note= "Xaa at position 42 is Gly,
Asp, Ser, Ala, Asn, Ile, Leu, Met, Tyr, or Arg"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 45
(D) OTHER INFORMATION: /note= "Xaa at position 45 is Gln,
Val, Met, Leu, Ala, Asn, Glu, or Lys"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 46
(D) OTHER INFORMATION: /note= "Xaa at position 46 is Asp,
Phe, Ser, Gln, Glu, His, Val, or Thr"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 50
(D) OTHER INFORMATION: /note= "Xaa at position 50 is Glu,
Asn, Ser, or Asp"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 51
(D) OTHER INFORMATION: /note= "Xaa at position 51 is Asn,
Arg, Pro, Thr, or His"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 55
(D) OTHER INFORMATION: /note= "Xaa at position 55 is Arg,
Leu, or Gly"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 56
(D) OTHER INFORMATION: /note= "Xaa at position 56 is Pro,
Gly, Ser, Ala, Asn, Val, Leu, or Gln"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 62



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Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser,
Thr, Tyr, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 87
- (D) OTHER INFORMATION: /note= "Xaa at position 87 is Leu
or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 88
- (D) OTHER INFORMATION: /note= "Xaa at position 88 is Ala
or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 91
- (D) OTHER INFORMATION: /note= "Xaa at position 91 is Ala
or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 93
- (D) OTHER INFORMATION: /note= "Xaa at position 93 is Thr,
Asp, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is His,
Pro, Arg, Val, Gly, Asn, Ser, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is His,
Ile, Asn, Ala, Thr, Gln, Glu, Lys, Met, Ser, Tyr,
Val, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 99
- (D) OTHER INFORMATION: /note= "Xaa at position 99 is Ile
or Leu"

(ix) FEATURE:

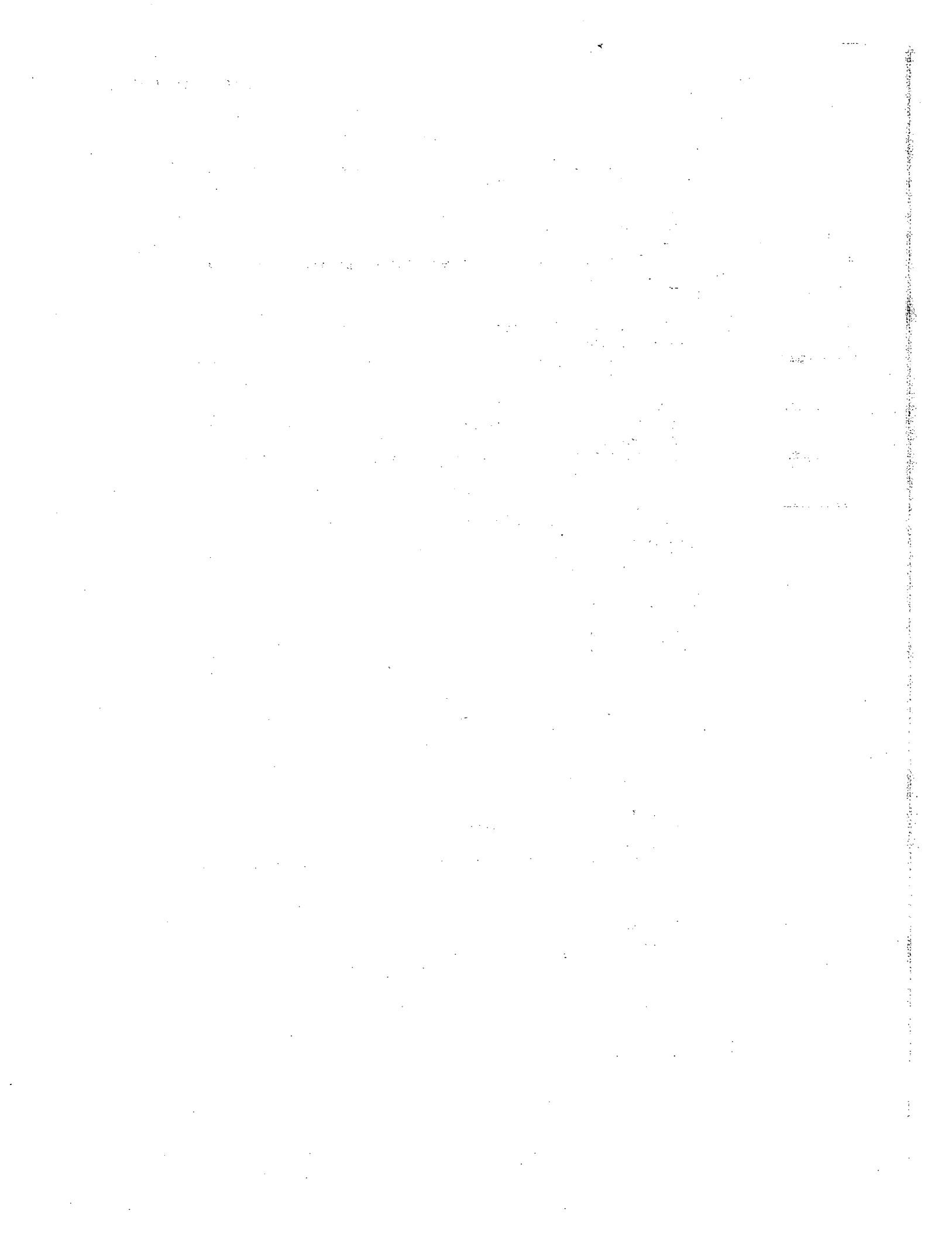
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys
or Arg"

(ix) FEATURE;

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp,
Pro, Met, Lys, Thr, His, Asn, Ile, Leu, or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 105



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Xaa Xaa Met Ile Asp Glu Xaa	Ile Xaa Xaa Leu Lys Xaa Xaa Pro Xaa		
20	25	30	
Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa Ile Leu			
35	40	45	
Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala Phe Xaa Arg Xaa			
50	55	60	
Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu Xaa Xaa Leu Xaa Xaa			
65	70	75	80
Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala Xaa Pro Xaa Arg Xaa Pro			
85	90	95	
Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa Glu Phe Xaa Xaa Lys Leu Xaa			
100	105	110	
Phe Tyr Leu Xaa Xaa Leu Glu Xaa Xaa Xaa Gln Gln Thr Thr Leu			
115	120	125	
Ser Leu Ala Ile Phe			
130			

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /note= "Met- or Met-Ala- may or may not precede the amino acid in position 1"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /note= "Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg"

(ix) FEATURE:

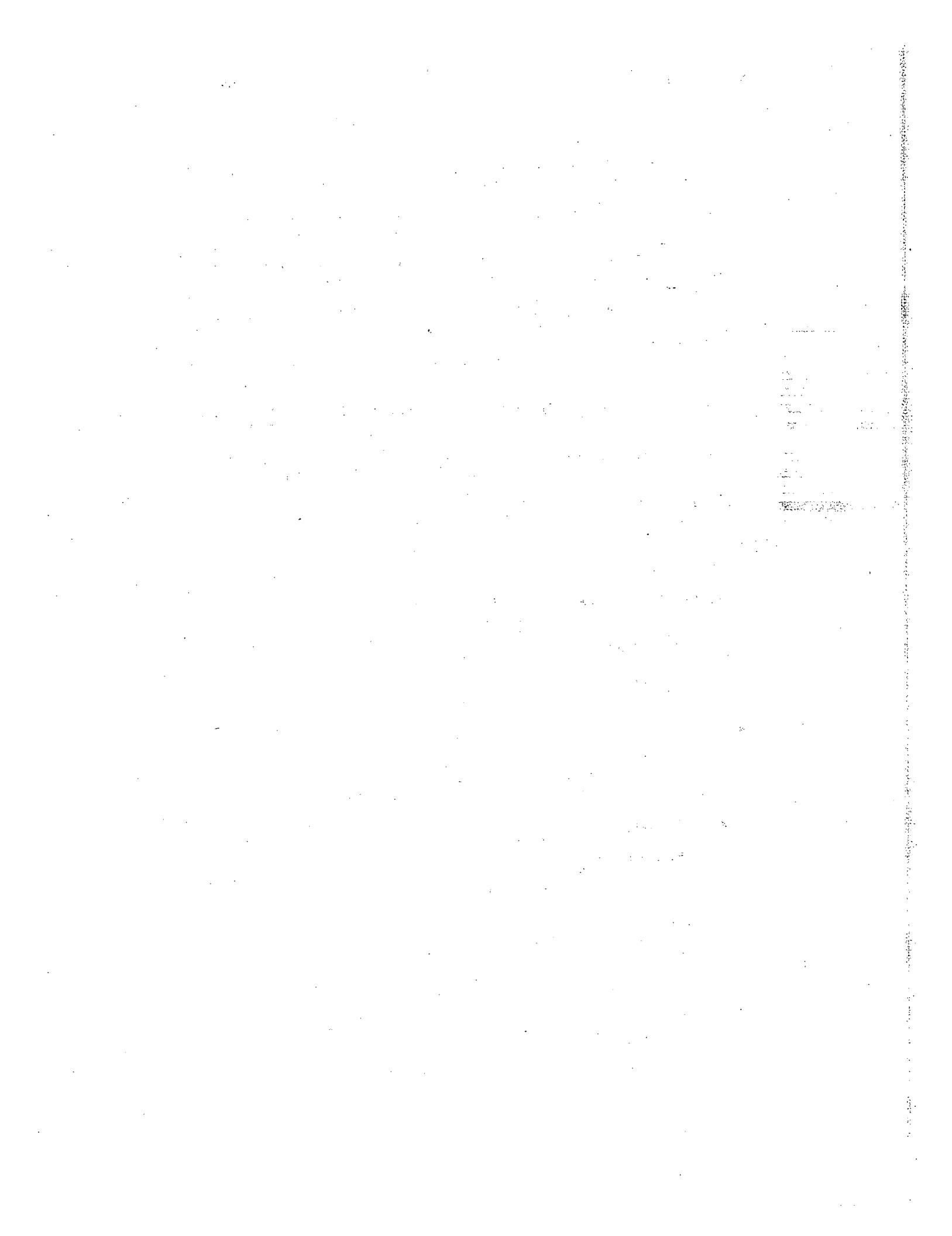
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /note= "Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /note= "Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys"

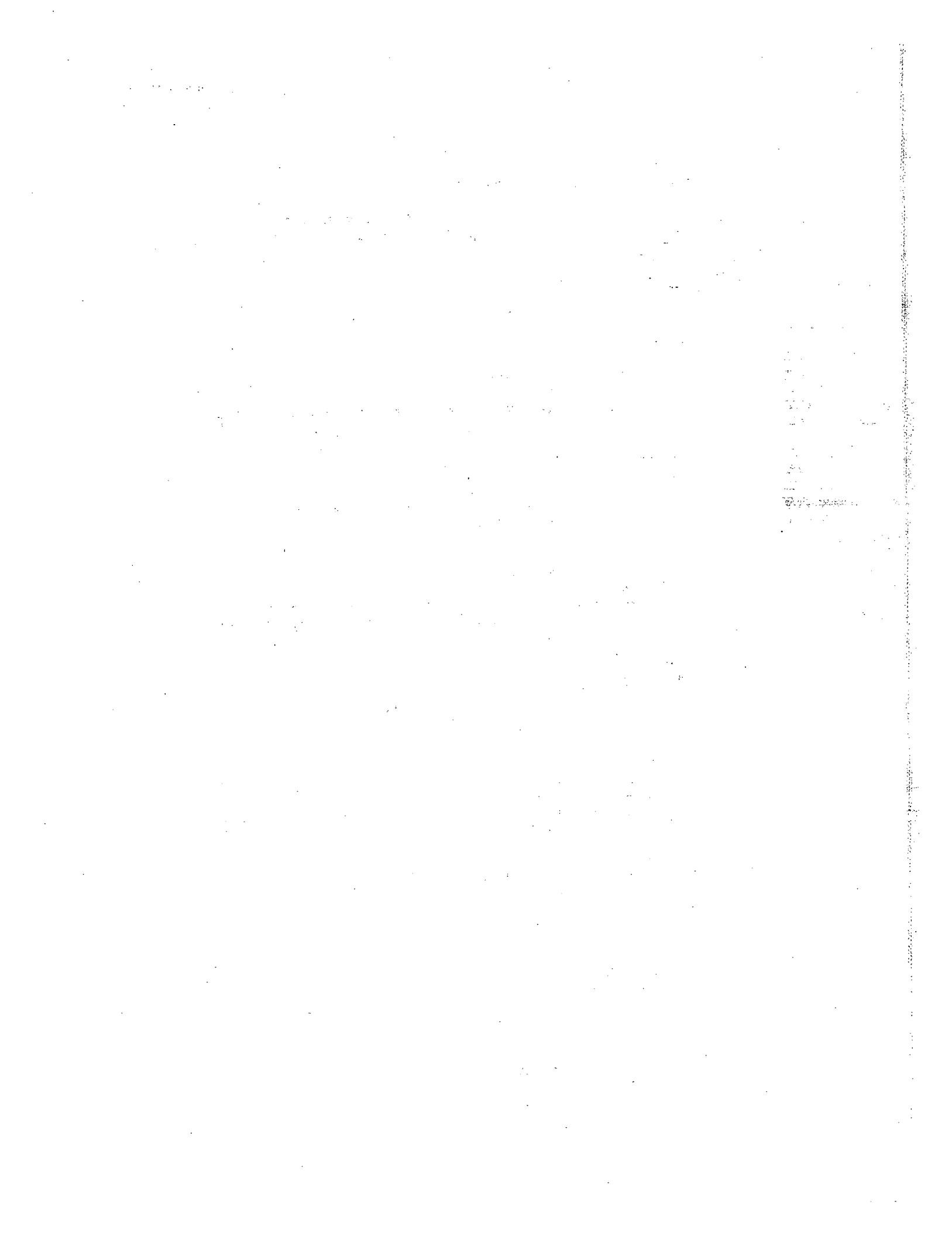
(ix) FEATURE:

- (A) NAME/KEY: Modified-site



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- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 16
(D) OTHER INFORMATION: /note= "Xaa at position 16 is Pro,
His, Thr, Gly, Asp, Gln, Ser, Leu, or Lys"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 17
(D) OTHER INFORMATION: /note= "Xaa at position 17 is Pro,
Asp, Gly, Ala, Arg, Leu, or Gln"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 18
(D) OTHER INFORMATION: /note= "Xaa at position 18 is Leu,
Val, Arg, Gln, Asn, Gly, Ala, or Glu"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 19
(D) OTHER INFORMATION: /note= "Xaa at position 19 is Pro,
Leu, Gln, Ala, Thr, or Glu"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 20
(D) OTHER INFORMATION: /note= "Xaa at position 20 is Leu,
Val, Gly, Ser, Lys, Glu, Gln, Thr, Arg, Ala, Phe,
Ile, or Met"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 21
(D) OTHER INFORMATION: /note= "Xaa at position 21 is Leu,
Ala, Gly, Asn, Pro, Gln, or Val"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 22
(D) OTHER INFORMATION: /note= "Xaa at position 22 is Asp,
Leu, or Val"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 23
(D) OTHER INFORMATION: /note= "Xaa at position 23 is Phe,
Ser, Pro, Trp, or Ile"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 24
(D) OTHER INFORMATION: /note= "Xaa at position 24 is Asn
or Ala"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 26
(D) OTHER INFORMATION: /note= "Xaa at position 26 is Leu,
Trp, or Arg"



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(A) NAME/KEY: Modified-site
(B) LOCATION: 36
(D) OTHER INFORMATION: /note= "Xaa at position 36 is Glu,
Leu, Thr, Asp, Tyr, Lys, Asn, Ser, Ala, Ile, Val,
His, Phe, Met, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 37
(D) OTHER INFORMATION: /note= "Xaa at position 37 is Asn,
Arg, Met, Pro, Ser, Thr, or His"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 38
(D) OTHER INFORMATION: /note= "Xaa at position 38 is Asn,
His, Arg, Leu, Gly, Ser, or Thr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 39
(D) OTHER INFORMATION: /note= "Xaa at position 39 is
Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or Met"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 40
(D) OTHER INFORMATION: /note= "Xaa at position 40 is Arg,
Asp, Ile, Ser, Val, Thr, Gln, Asn, Lys, His,
Ala, or Leu"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 41
(D) OTHER INFORMATION: /note= "Xaa at position 41 is Arg,
Thr, Val, Ser, Leu, or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 42
(D) OTHER INFORMATION: /note= "Xaa at position 42 is Pro,
Gly, Cys, Ser, Gln, Glu, Arg, His, Thr, Ala, Tyr,
Phe, Leu, Val, or Lys"

(ix) FEATURE:

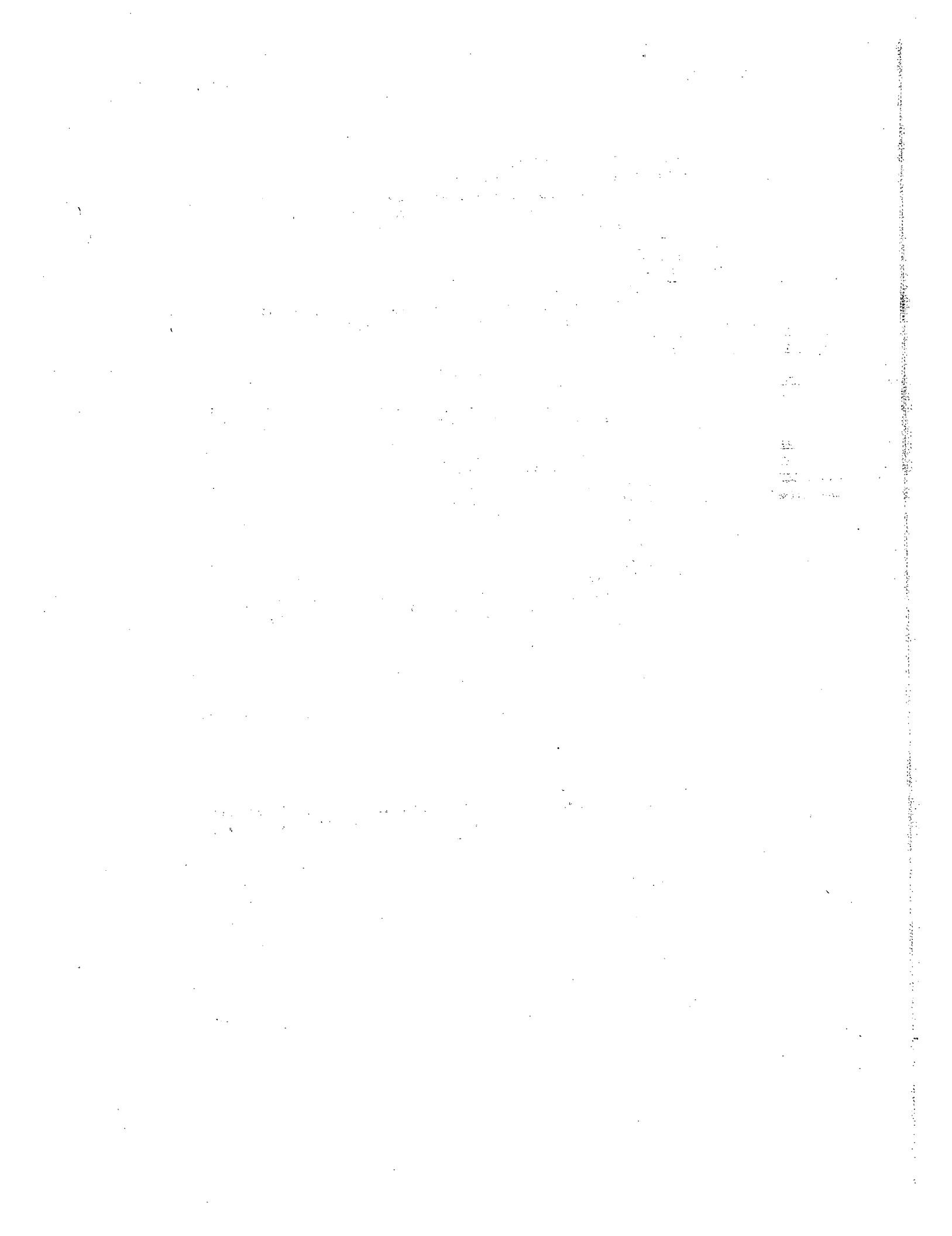
(A) NAME/KEY: Modified-site
(B) LOCATION: 43
(D) OTHER INFORMATION: /note= "Xaa at position 43 is Asn
or Gly"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 44
(D) OTHER INFORMATION: /note= "Xaa at position 44 is Leu,
Ser, Asp, Arg, Gln, Val, or Cys"

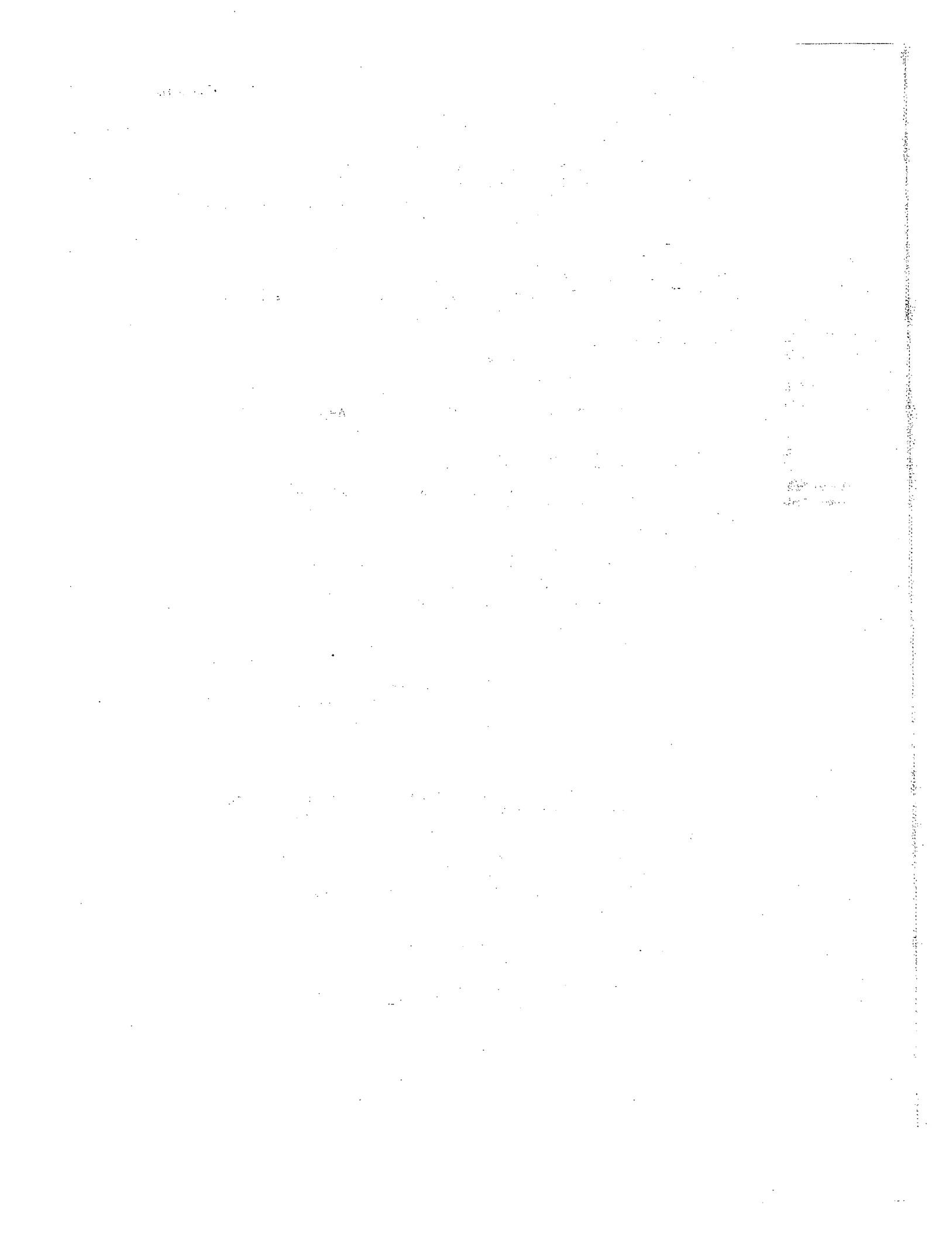
(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 45
(D) OTHER INFORMATION: /note= "Xaa at position 45 is Glu,
Tyr, His, Leu, Pro, or Arg"



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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 56
- (D) OTHER INFORMATION: /note= "Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 57
 - (D) OTHER INFORMATION: /note= "Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, Trp, or Asn"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 58
 - (D) OTHER INFORMATION: /note= "Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 59
 - (D) OTHER INFORMATION: /note= "Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 60
 - (D) OTHER INFORMATION: /note= "Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 61
 - (D) OTHER INFORMATION: /note= "Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln, or Leu"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 62
 - (D) OTHER INFORMATION: /note= "Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or Asp"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 63
 - (D) OTHER INFORMATION: /note= "Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 64
 - (D) OTHER INFORMATION: /note= "Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 65
 - (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile, or Asp"
- (ix) FEATURE:



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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 76
- (D) OTHER INFORMATION: /note= "Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or Met"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 77
 - (D) OTHER INFORMATION: /note= "Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 78
 - (D) OTHER INFORMATION: /note= "Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, Ile, or Leu"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 79
 - (D) OTHER INFORMATION: /note= "Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 80
 - (D) OTHER INFORMATION: /note= "Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, His, Ala, or Pro"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 81
 - (D) OTHER INFORMATION: /note= "Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 82
 - (D) OTHER INFORMATION: /note= "Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 83
 - (D) OTHER INFORMATION: /note= "Xaa at position 83 is Ile, Val, Lys, Ala, or Asn"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 84
 - (D) OTHER INFORMATION: /note= "Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr, Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr, or Pro"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 85
 - (D) OTHER INFORMATION: /note= "Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln, Gly, Ser, Phe, or His"

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Asn, Thr, Leu, Gln, Arg, His, Glu, Ser, Ala,
or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 97
- (D) OTHER INFORMATION: /note= "Xaa at position 97 is Leu,
Ile, Arg, Asp, or Met"

{ (ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is Thr,
Val, Gln, Tyr, Glu, His, Ser, or Phe"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 99
- (D) OTHER INFORMATION: /note= "Xaa at position 99 is Phe,
Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile,
Val, or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100
- (D) OTHER INFORMATION: /note= "Xaa at position 100 is Tyr,
Cys, His, Ser, Trp, Arg, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101
- (D) OTHER INFORMATION: /note= "Xaa at position 101 is Leu,
Asn, Val, Pro, Arg, Ala, His, Thr, Trp, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 102
- (D) OTHER INFORMATION: /note= "Xaa at position 102 is
Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, Arg, Trp,
Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 103
- (D) OTHER INFORMATION: /note= "Xaa at position 103 is Thr,
Ser, Asn, Ile, Trp, Lys, or Pro"

(ix) FEATURE:

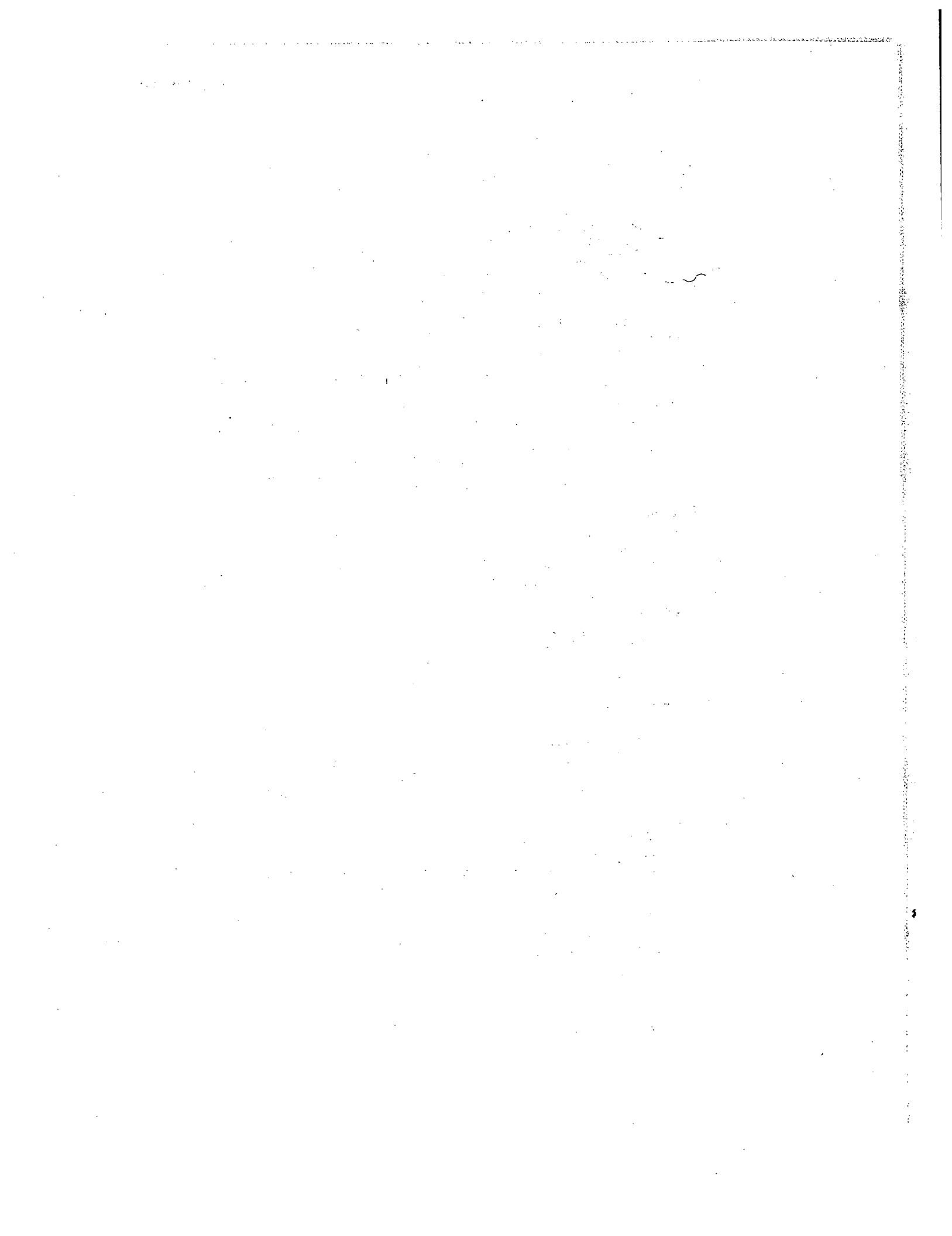
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 104
- (D) OTHER INFORMATION: /note= "Xaa at position 104 is Leu,
Ser, Pro, Ala, Glu, Cys, Asp, or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 105
- (D) OTHER INFORMATION: /note= "Xaa at position 105 is Glu,
Ser, Lys, Pro, Leu, Thr, Tyr, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site



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not precede the amino acid in position 1"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 3
- (D) OTHER INFORMATION: /note= "Xaa at position 3 is Ser,
Gly, Asp, Met, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /note= "Xaa at position 4 is Asn,
His, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /note= "Xaa at position 5 is Met
or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 7
- (C) OTHER INFORMATION: /note= "Xaa at position 7 is Asp or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /note= "Xaa at position 9 is Ile,
Ala, Leu, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 10
- (D) OTHER INFORMATION: /note= "Xaa at position 10 is Ile,
Val, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /note= "Xaa at position 11 is Thr,
His, Gln, or Ala"

(ix) FEATURE:

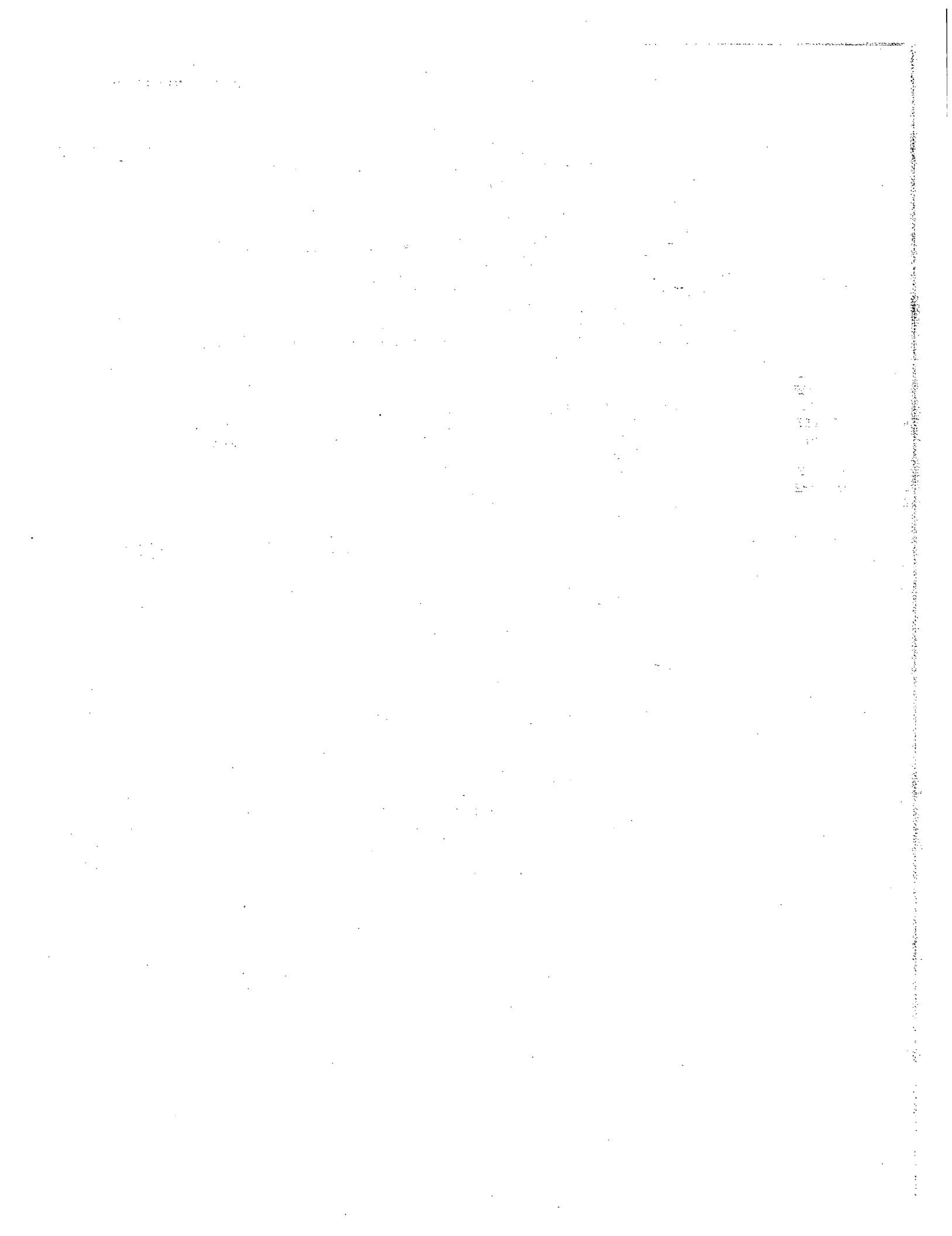
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /note= "Xaa at position 12 is His
or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /note= "Xaa at position 15 is Gln,
Asn, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /note= "Xaa at position 16 is Pro,
Gly, or Gln"



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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 32
- (D) OTHER INFORMATION: /note= "Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln, Glu, His, Ile, Lys, Tyr, Val, or Cys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 36
- (D) OTHER INFORMATION: /note= "Xaa at position 36 is Glu, Ala, Asn, Ser, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 37
- (D) OTHER INFORMATION: /note= "Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 40
- (D) OTHER INFORMATION: /note= "Xaa at position 40 is Arg or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 41
- (D) OTHER INFORMATION: /note= "Xaa at position 41 is Arg, Thr, Val, Leu, or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 42
- (D) OTHER INFORMATION: /note= "Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn, Glu, Leu, Thr, Val, or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Ala or Ser"

(ix) FEATURE:

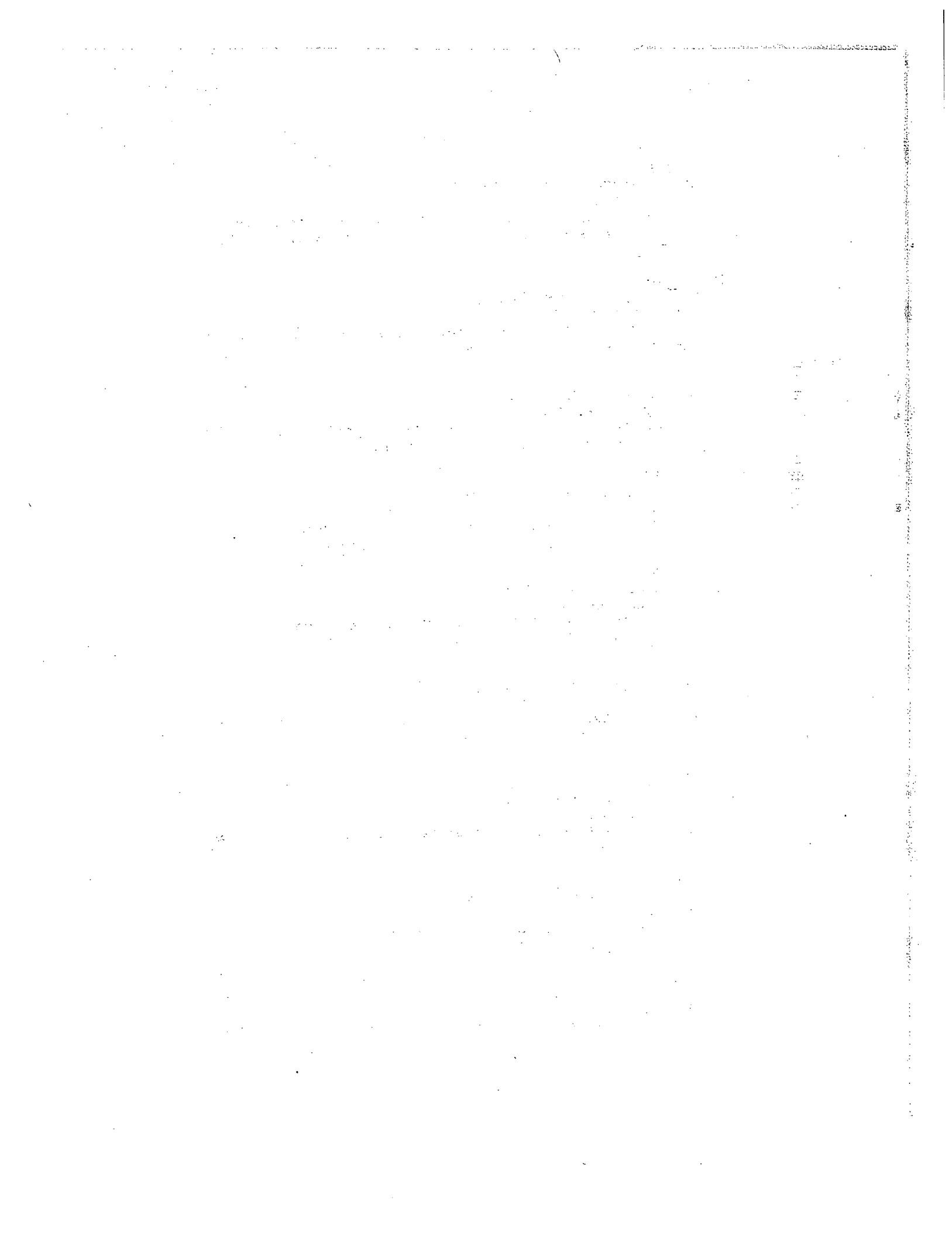
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 48
- (D) OTHER INFORMATION: /note= "Xaa at position 48 is Asn, Pro, Thr, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 49
- (D) OTHER INFORMATION: /note= "Xaa at position 49 is Arg or Lys"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 50
- (D) OTHER INFORMATION: /note= "Xaa at position 50 is Ala or Asn"



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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile, Gly, or Asp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 66
- (D) OTHER INFORMATION: /note= "Xaa at position 66 is Asn, Gly, Glu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68
- (D) OTHER INFORMATION: /note= "Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn, Glu, His, Ile, Met, Phe, Ser, Thr, Tyr, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 69
- (D) OTHER INFORMATION: /note= "Xaa at position 69 is Pro or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 71
- (D) OTHER INFORMATION: /note= "Xaa at position 71 is Leu or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 73
- (D) OTHER INFORMATION: /note= "Xaa at position 73 is Leu or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 74
- (D) OTHER INFORMATION: /note= "Xaa at position 74 is Ala or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 77
- (D) OTHER INFORMATION: /note= "Xaa at position 77 is Ala or Pro"

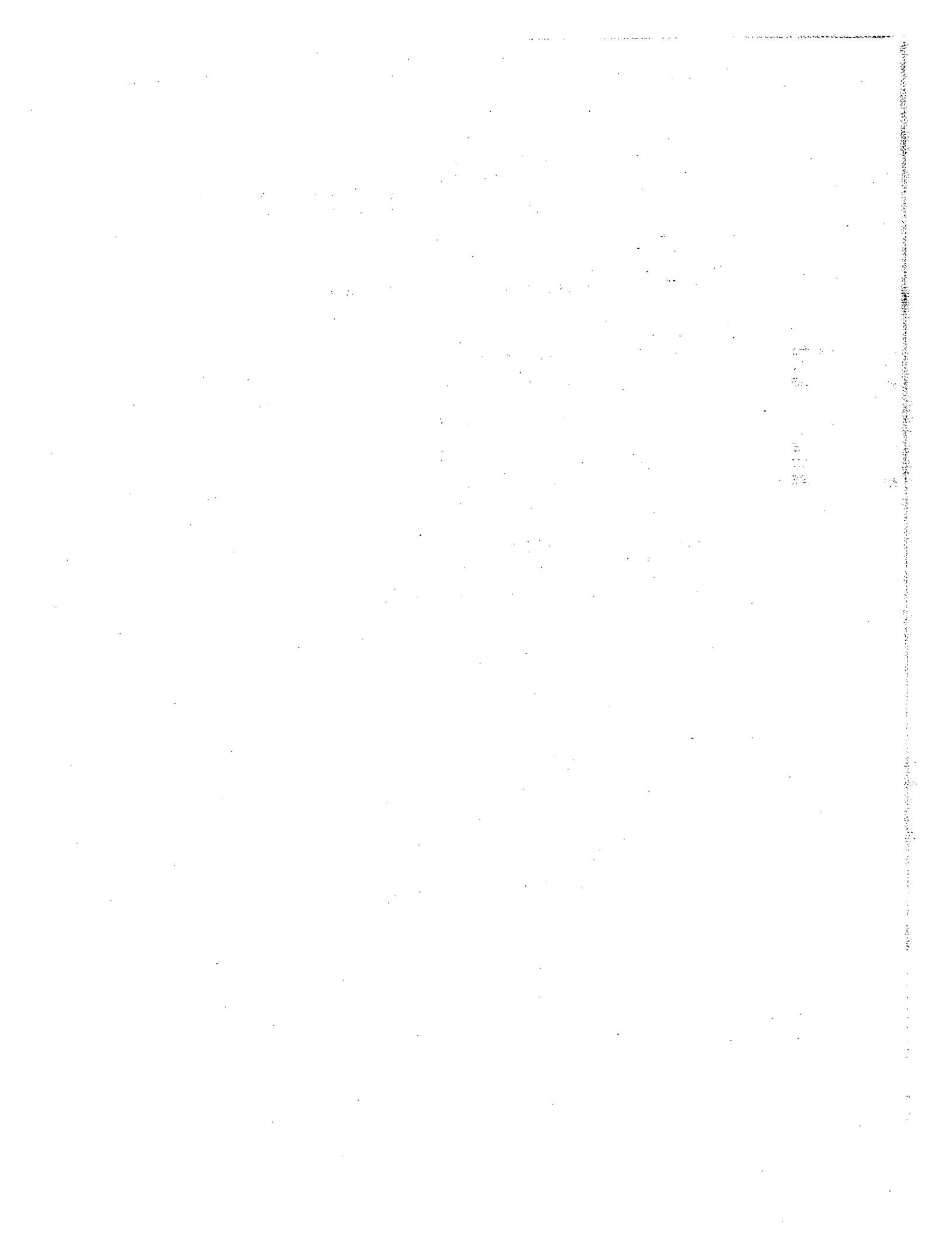
(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 79
- (D) OTHER INFORMATION: /note= "Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 81
- (D) OTHER INFORMATION: /note= "Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn, Phe, Ser, or Thr"

(ix) FEATURE:



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(A) NAME/KEY: Modified-site
(B) LOCATION: 95
(D) OTHER INFORMATION: /note= "Xaa at position 95 is Arg,
Thr, Glu, Leu, or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 98
(D) OTHER INFORMATION: /note= "Xaa at position 98 is Thr,
Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 100
(D) OTHER INFORMATION: /note= "Xaa at position 100 is Tyr
or Trp"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 101
(D) OTHER INFORMATION: /note= "Xaa at position 101 is Leu
or Ala"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 102
(D) OTHER INFORMATION: /note= "Xaa at position 102 is Lys,
Thr, Val, Trp, Ser, Ala, His, Met, Phe, Tyr, or Ile"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 103
(D) OTHER INFORMATION: /note= "Xaa at position 103 is Thr
or Ser"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 106
(D) OTHER INFORMATION: /note= "Xaa at position 106 is Asn,
Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 107
(D) OTHER INFORMATION: /note= "Xaa at position 107 is Ala,
Ser, Ile, Asn, Pro, Asp, or Gly"

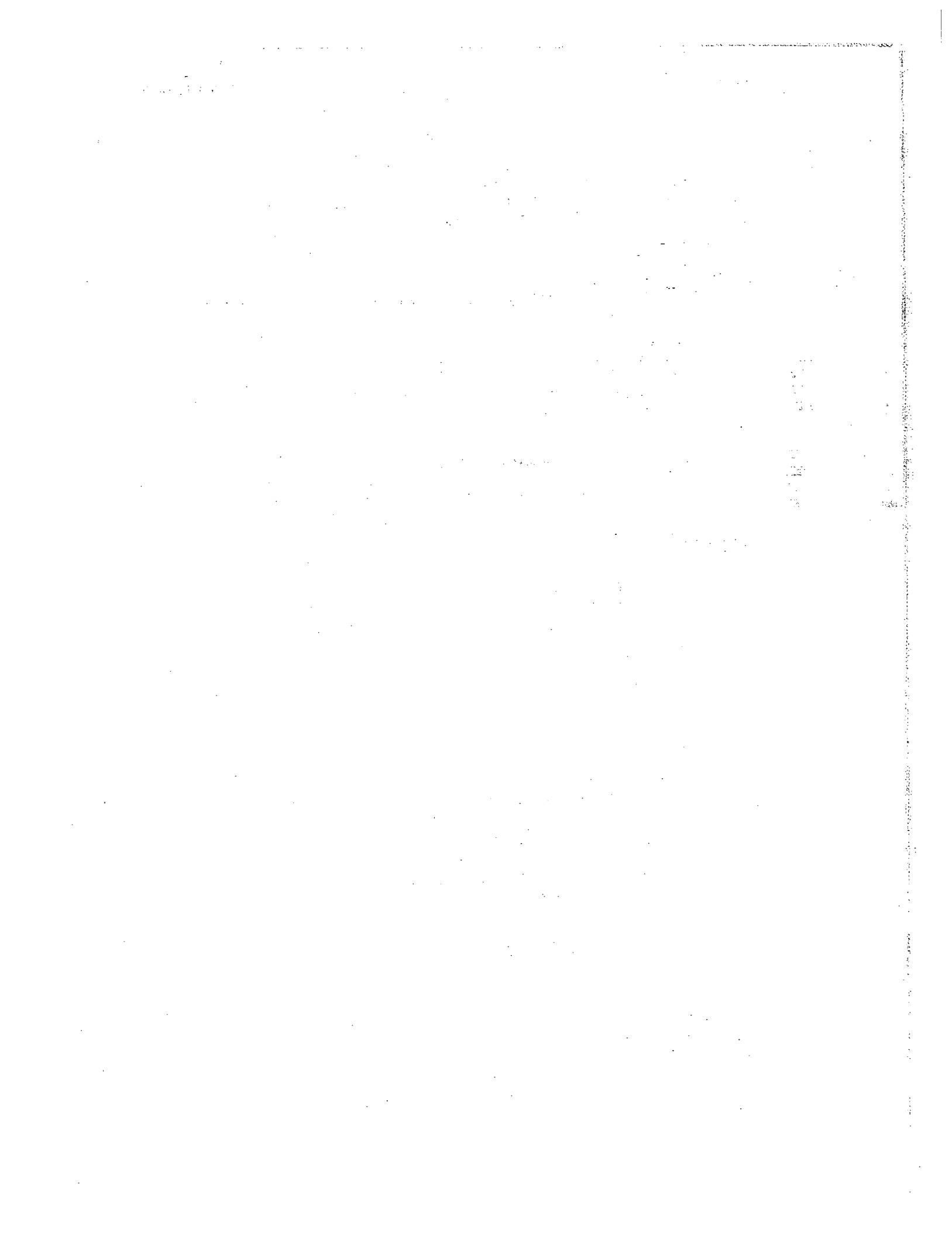
(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 108
(D) OTHER INFORMATION: /note= "Xaa at position 108 is Gln,
Ser, Met, Trp, Arg, Phe, Pro, His, Ile, Tyr, or Cys"

(ix) FEATURE:

(A) NAME/KEY: Modified-site
(B) LOCATION: 109
(D) OTHER INFORMATION: /note= "Xaa at position 109 is Ala,
Met, Glu, His, Ser, Pro, Tyr, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:



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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 12
- (D) OTHER INFORMATION: /note= "Xaa at position 12 is His or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /note= "Xaa at position 15 is Gln or Asn"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 16
- (D) OTHER INFORMATION: /note= "Xaa at position 16 is Pro or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Leu, Arg, Asn, or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 21
- (D) OTHER INFORMATION: /note= "Xaa at position 21 is Leu, Ala, Asn, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 24
- (D) OTHER INFORMATION: /note= "Xaa at position 24 is Asn or Ala"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 28
- (D) OTHER INFORMATION: /note= "Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu, Met, Tyr, or Arg"

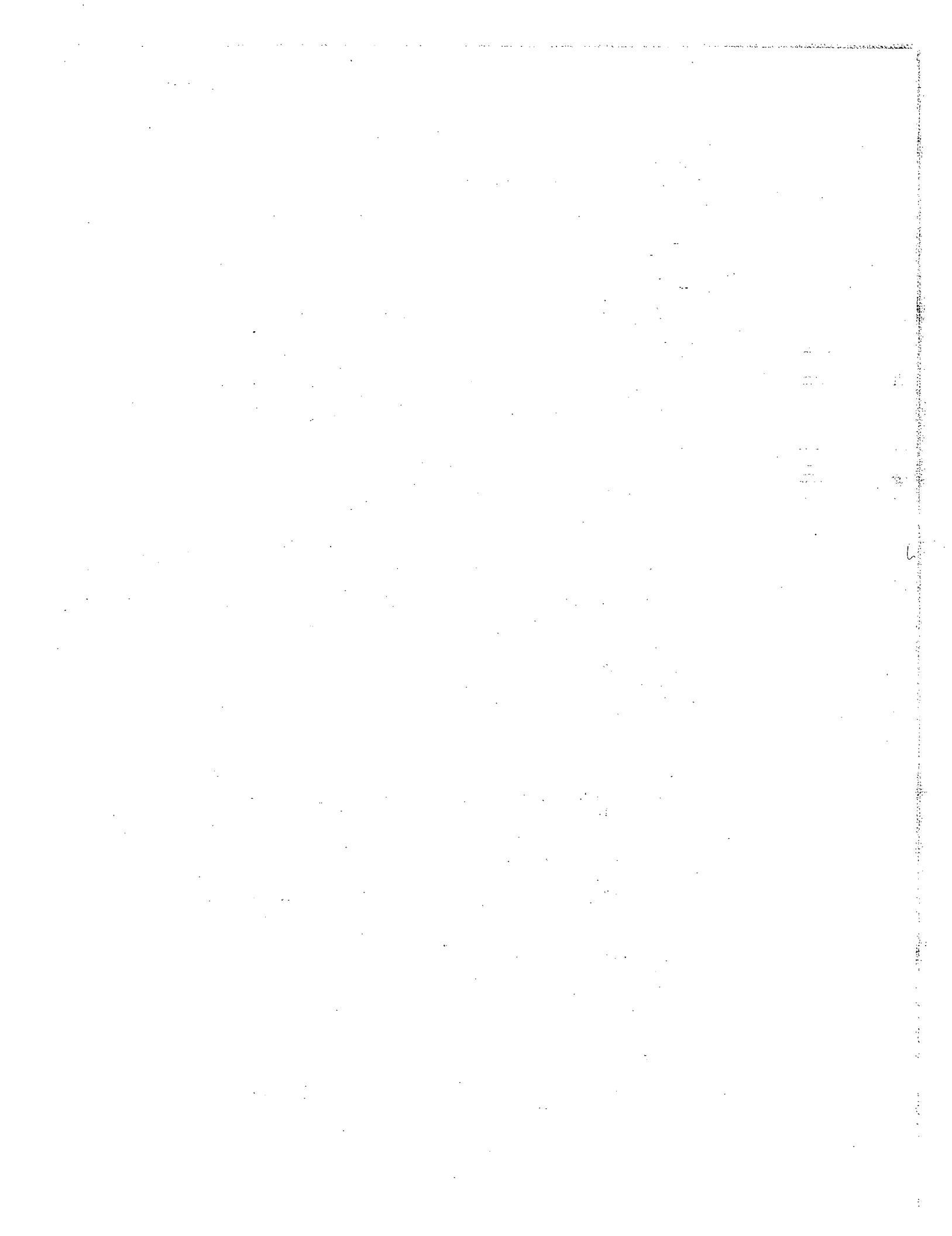
(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 31
- (D) OTHER INFORMATION: /note= "Xaa at position 31 is Gln, Val, Met, Leu, Ala, Asn, Glu, or Lys"

(ix) FEATURE:

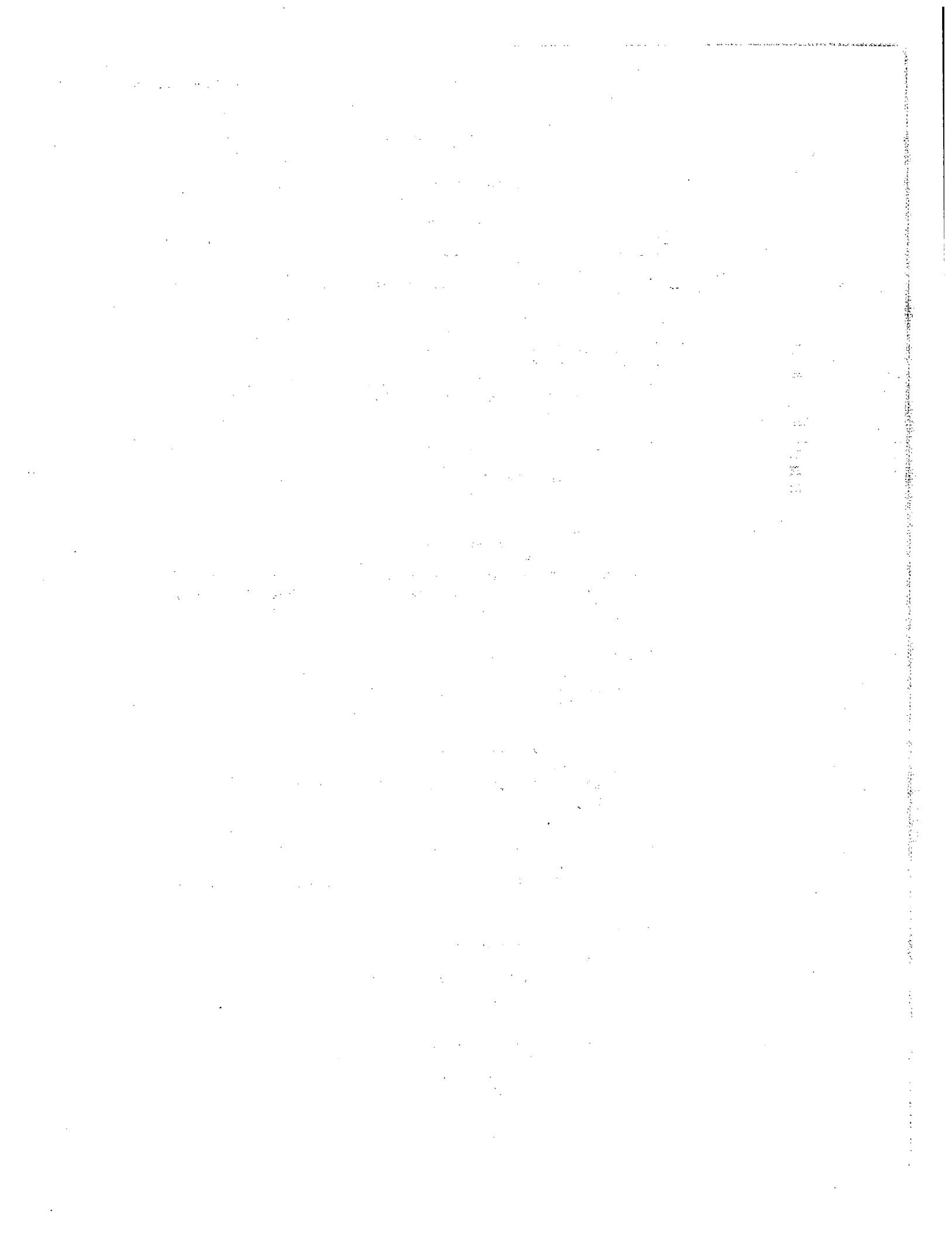
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 32
- (D) OTHER INFORMATION: /note= "Xaa at position 32 is Asp, Phe, Ser, Ala, Gln, Glu, His, Val, or Thr"

(ix) FEATURE:



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- (B) LOCATION: 62
(D) OTHER INFORMATION: /note= "Xaa at position 62 is Ser,
Val, Asn, Pro, or Gly"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 63
(D) OTHER INFORMATION: /note= "Xaa at position 63 is Ile
or Leu"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 65
(D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys,
Asn, Met, Arg, Ile, or Gly"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 66
(D) OTHER INFORMATION: /note= "Xaa at position 66 is Asn,
Gly, Glu, or Arg"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 68
(D) OTHER INFORMATION: /note= "Xaa at position 68 is Leu,
Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser,
Thr, Tyr, or Val"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 73
(D) OTHER INFORMATION: /note= "Xaa at position 73 is Leu
or Ser"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 74
(D) OTHER INFORMATION: /note= "Xaa at position 74 is Ala
or Trp"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 77
(D) OTHER INFORMATION: /note= "Xaa at position 77 is Ala
or Pro"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 79
(D) OTHER INFORMATION: /note= "Xaa at position 79 is Thr,
Asp, or Ala"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site
(B) LOCATION: 81
(D) OTHER INFORMATION: /note= "Xaa at position 81 is His,
Pro, Arg, Val, Gly, Asn, Ser, or Thr"
- (ix) FEATURE:
(A) NAME/KEY: Modified-site



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(B) LOCATION: 106

(D) OTHER INFORMATION: /note= "Xaa at position 106 is Asn,
Pro, Leu, His, Val, or Gln"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 107

(D) OTHER INFORMATION: /note= "Xaa at position 107 is Ala,
Ser, Ile, Pro, or Asn"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 108

(D) OTHER INFORMATION: /note= "Xaa at position 108 is Gln,
Met, Trp, Phe, Pro, His, Ile or Tyr"

(ix) FEATURE:

(A) NAME/KEY: Modified-site

(B) LOCATION: 109

(D) OTHER INFORMATION: /note= "Xaa at position 109 is Ala,
Met, Glu, Ser, or Leu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6.

Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa
20 25 30

Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala Phe Xaa
35 40 45

Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu Xaa Xaa Leu
50 55 60

Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala Xaa Pro Xaa Arg
65 70 75 80

Xaa Pro Ile Xaa Xaa Xaa Gly Asp Trp Xaa Glu Phe Xaa Xaa Lys
85 90 95

Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa Xaa Xaa Xaa Gln Gln
100 105 110

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS.

SEQUENCE CHARACTERISTICS:
(A) LENGTH: 133 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

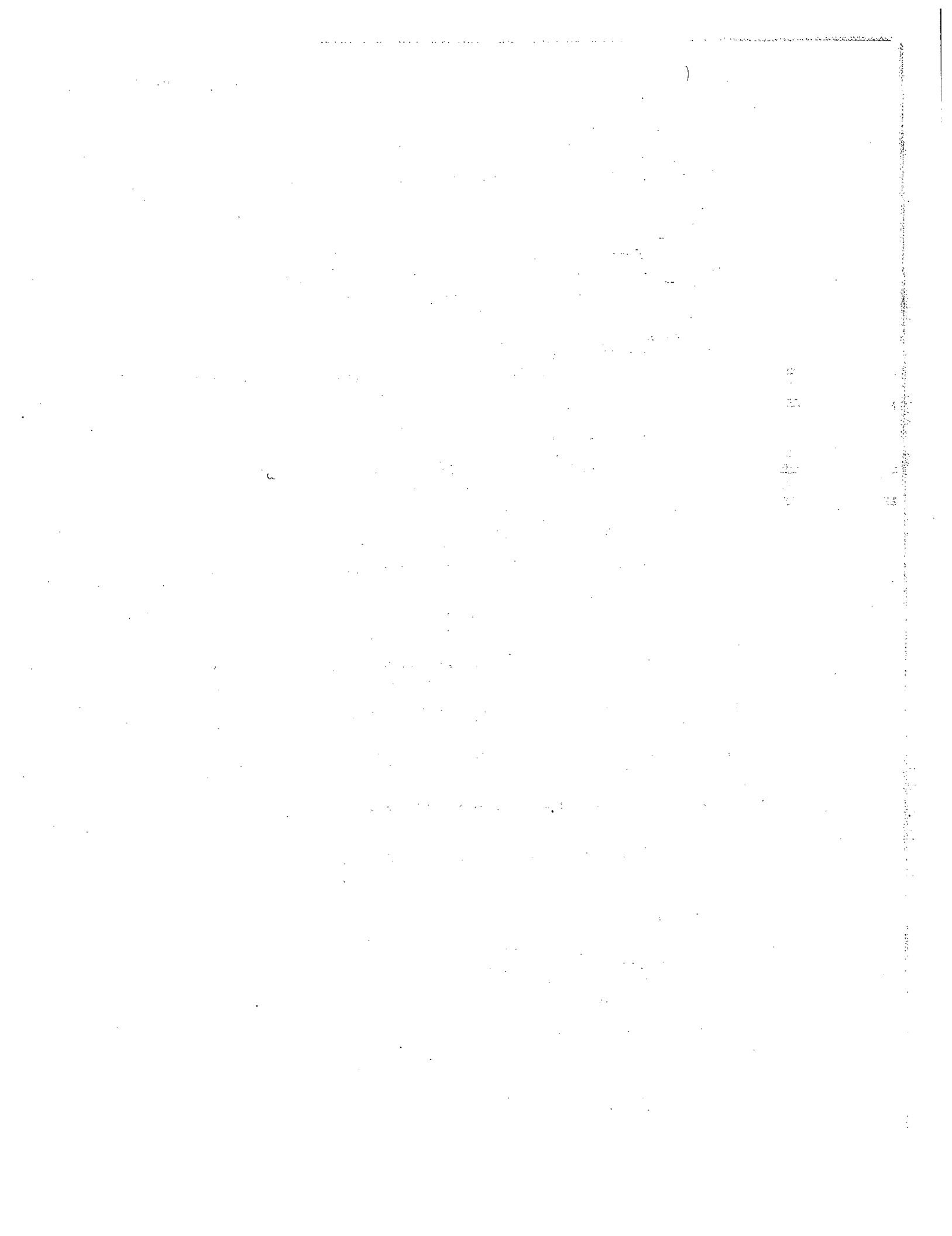
(ii) MOLECULE TYPE: peptide

(ix) FEATURES.

(A) NAME/KEY: Medication

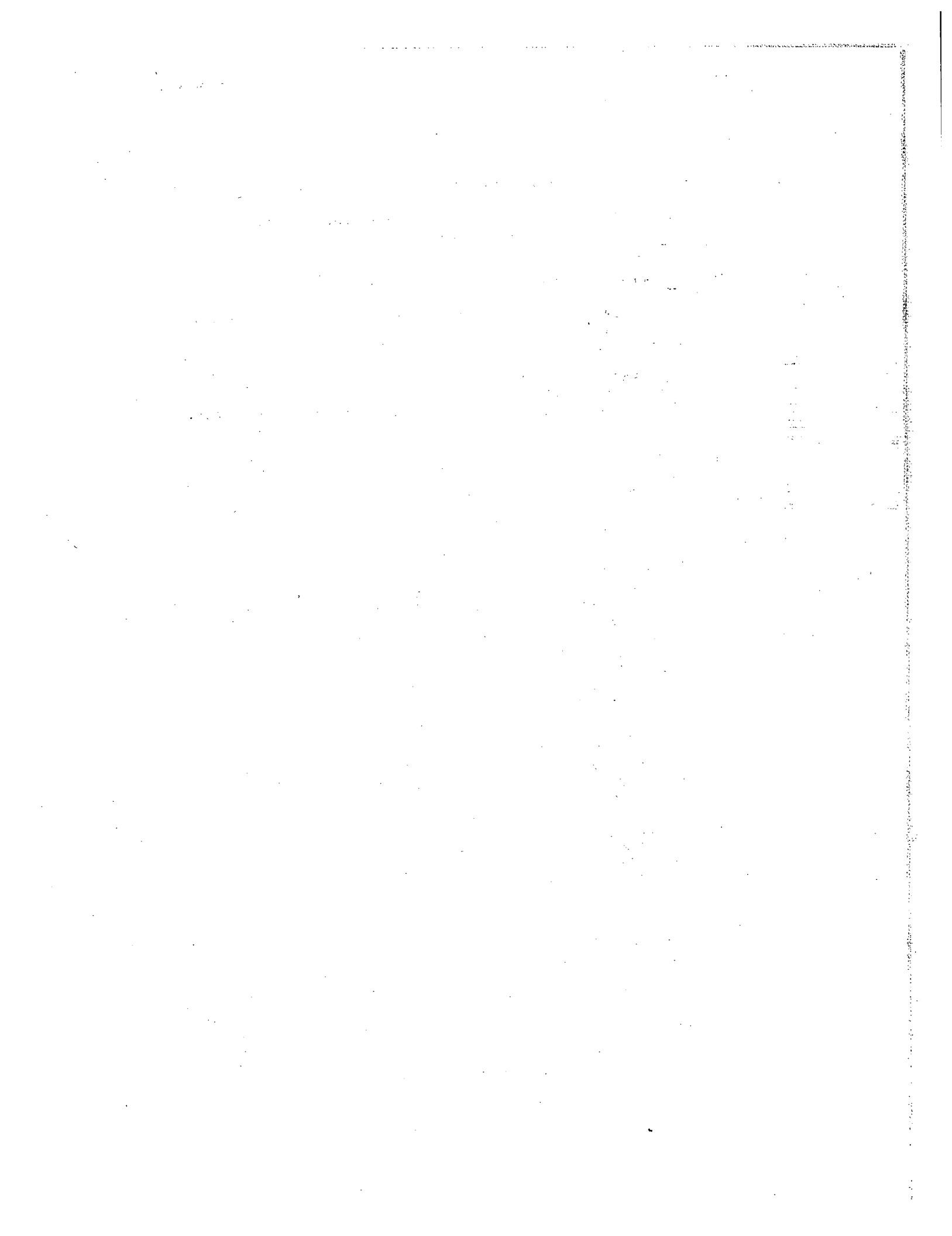
(A) NAME/KEY: Mc
(B) LOCATION: 1

(D) OTHER INFORMATION: /note= "Met- may or may not precede



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- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 42
 - (D) OTHER INFORMATION: /note= "Xaa at position 42 is Gly, Ala, Ser, Asp, or Asn"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 45
 - (D) OTHER INFORMATION: /note= "Xaa at position 45 is Gln, Val, or Met"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 46
 - (D) OTHER INFORMATION: /note= "Xaa at position 46 is Asp or Ser"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 49
 - (D) OTHER INFORMATION: /note= "Xaa at position 49 is Met, Ile, Leu, or Asp"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 50
 - (D) OTHER INFORMATION: /note= "Xaa at position 50 is Glu or Asp"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 51
 - (D) OTHER INFORMATION: /note= "Xaa at position 51 is Asn, Arg, or Ser"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 55
 - (D) OTHER INFORMATION: /note= "Xaa at position 55 is Arg, Leu, or Thr"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 56
 - (D) OTHER INFORMATION: /note= "Xaa at position 56 is Pro or Ser"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 59
 - (D) OTHER INFORMATION: /note= "Xaa at position 59 is Glu or Leu"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site
 - (B) LOCATION: 60
 - (D) OTHER INFORMATION: /note= "Xaa at position 60 is Ala or Ser"
- (ix) FEATURE:
 - (A) NAME/KEY: Modified-site



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(D) OTHER INFORMATION: /note= "Xaa at position 87 is Leu,
Ser, or Tyr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 88

(D) OTHER INFORMATION: /note= "Xaa at position 88 is Ala
or Trp"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 91

(D) OTHER INFORMATION: /note= "Xaa at position 91 is Ala
or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 93

(D) OTHER INFORMATION: /note= "Xaa at position 93 is Pro
or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95

(D) OTHER INFORMATION: /note= "Xaa at position 95 is His
or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98

(D) OTHER INFORMATION: /note= "Xaa at position 98 is His,
Ile, or Thr"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 100

(D) OTHER INFORMATION: /note= "Xaa at position 100 is Lys
or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 101

(D) OTHER INFORMATION: /note= "Xaa at position 101 is Asp,
Ala, or Met"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 105

(D) OTHER INFORMATION: /note= "Xaa at position 105 is Asn
or Glu"

(ix) FEATURE:

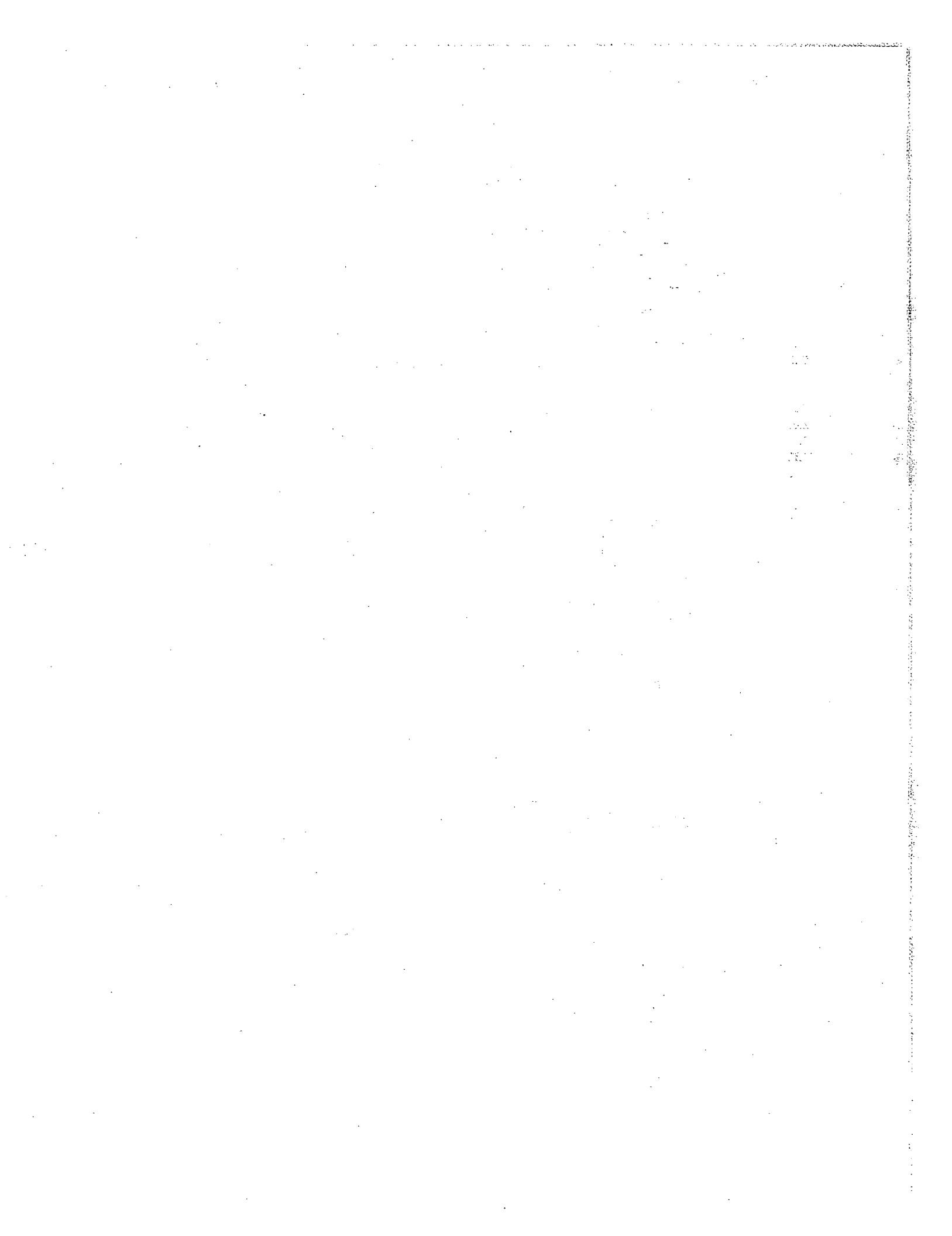
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 109

(D) OTHER INFORMATION: /note= "Xaa at position 109 is Arg,
Glu, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 112

(D) OTHER INFORMATION: /note= "Xaa at position 112 is Thr
or Gln"



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(ii) MOLECULE TYPE: peptide

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 1
- (D) OTHER INFORMATION: /note= "Met- or Met-Ala may or may not precede the amino acid in position 1"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 4
- (D) OTHER INFORMATION: /note= "Xaa at position 4 is Asn or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 5
- (D) OTHER INFORMATION: /note= "Xaa at position 5 is Met, Ala, or Ile"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 6
- (D) OTHER INFORMATION: /note= "Xaa at position 6 is Ile, Pro, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 9
- (D) OTHER INFORMATION: /note= "Xaa at position 9 is Ile, Ala, or Leu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 11
- (D) OTHER INFORMATION: /note= "Xaa at position 11 is Thr or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 15
- (D) OTHER INFORMATION: /note= "Xaa at position 15 is Gln, Arg, Val, or Ile"

(ix) FEATURE:

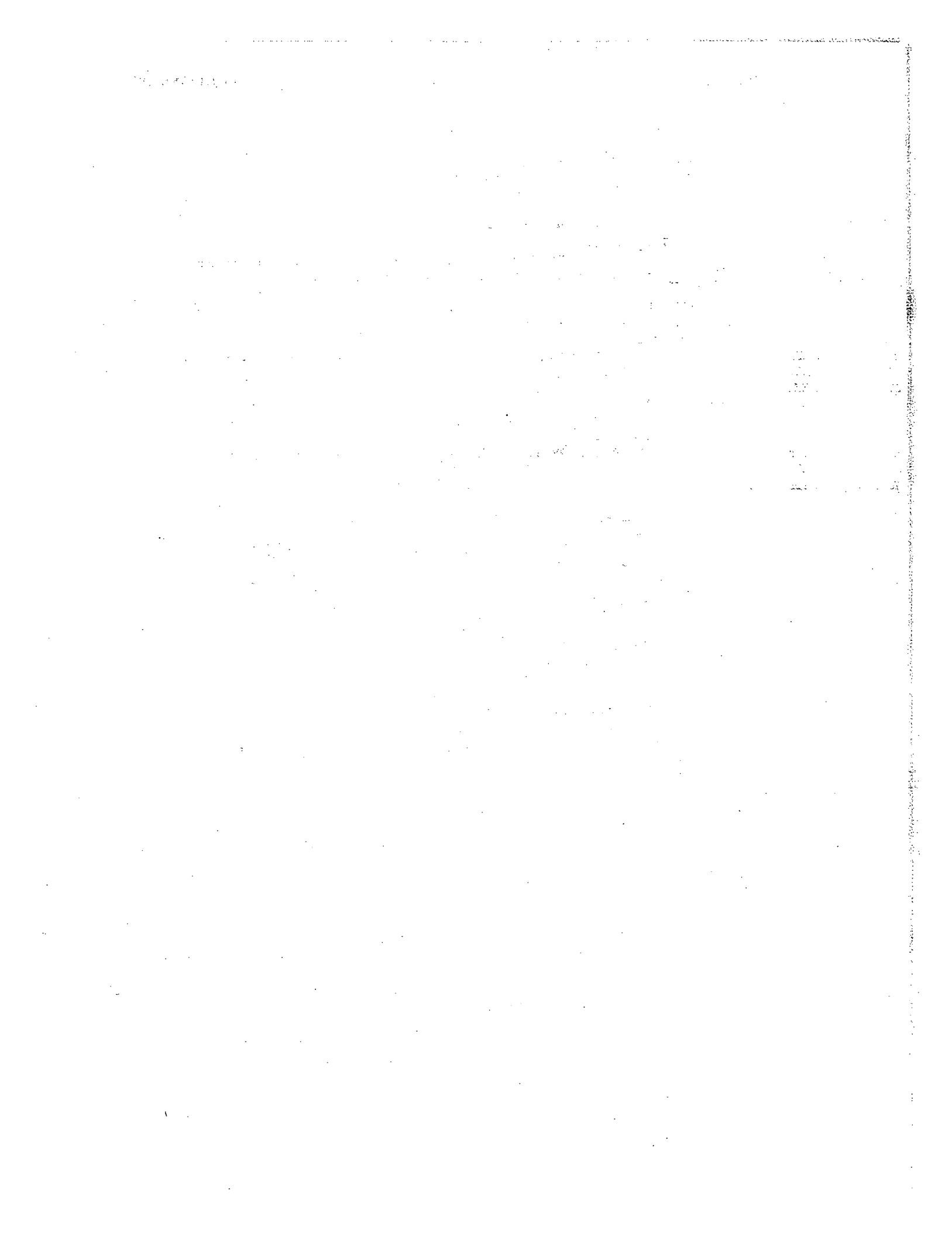
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 18
- (D) OTHER INFORMATION: /note= "Xaa at position 18 is Leu, Ala, Asn, or Arg"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 20
- (D) OTHER INFORMATION: /note= "Xaa at position 20 is Leu or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 23
- (D) OTHER INFORMATION: /note= "Xaa at position 23 is Phe,"



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- (A) NAME/KEY: Modified-site
- (B) LOCATION: 46
- (D) OTHER INFORMATION: /note= "Xaa at position 46 is Ala or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 48
- (D) OTHER INFORMATION: /note= "Xaa at position 48 is Asn, Val, or Pro"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 49
- (D) OTHER INFORMATION: /note= "Xaa at position 49 is Arg or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 51
- (D) OTHER INFORMATION: /note= "Xaa at position 51 is Val or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 53
- (D) OTHER INFORMATION: /note= "Xaa at position 53 is Ser, Asn, His, or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 55
- (D) OTHER INFORMATION: /note= "Xaa at position 55 is Gln or Glu"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 59
- (D) OTHER INFORMATION: /note= "Xaa at position 59 is Ala or Gly"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 62
- (D) OTHER INFORMATION: /note= "Xaa at position 62 is Ser, Ala, or Pro"

(ix) FEATURE:

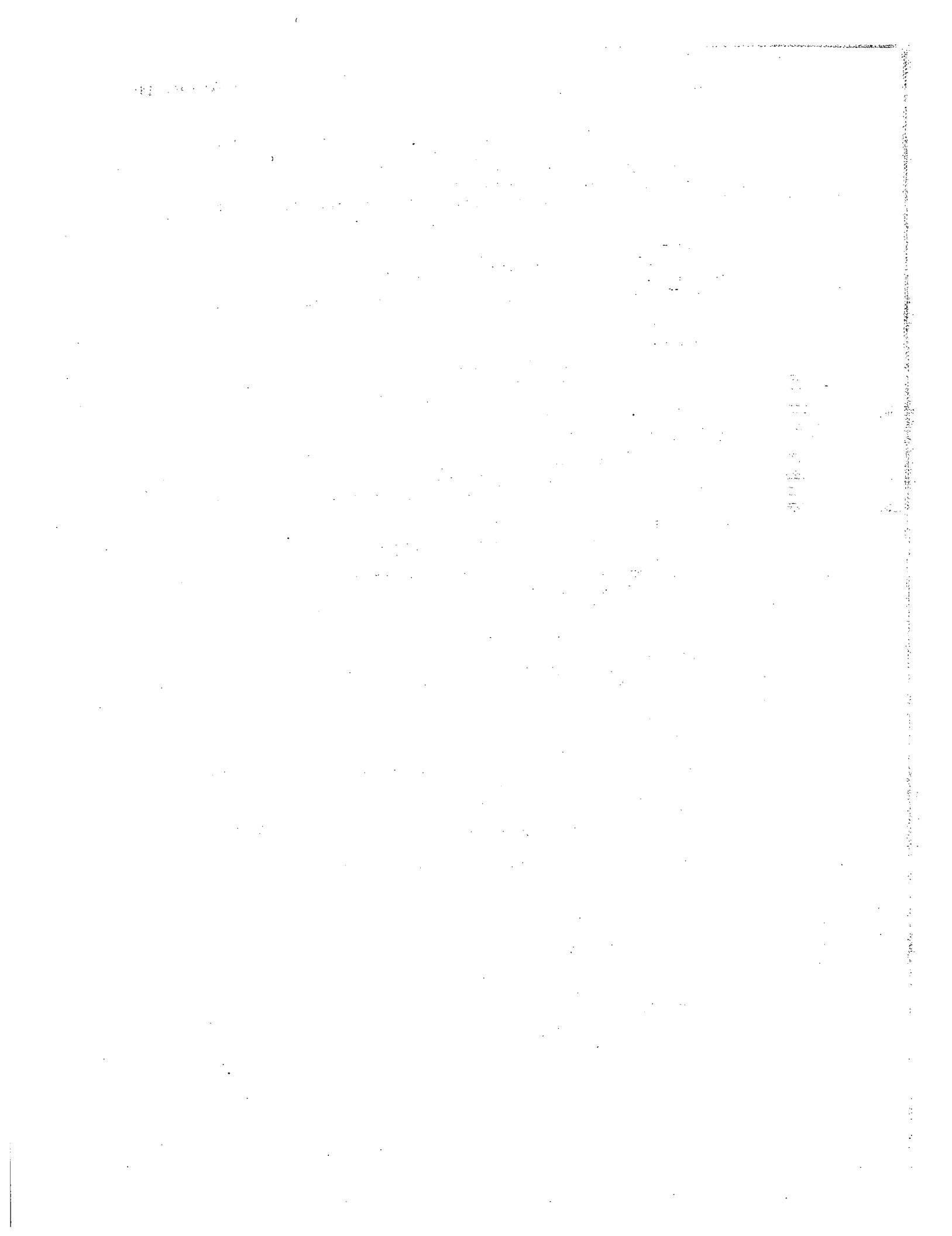
- (A) NAME/KEY: Modified-site
- (B) LOCATION: 65
- (D) OTHER INFORMATION: /note= "Xaa at position 65 is Lys, Arg, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 67
- (D) OTHER INFORMATION: /note= "Xaa at position 67 is Leu, Glu, or Val"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 68



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(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 95
- (D) OTHER INFORMATION: /note= "Xaa at position 95 is Arg, Glu, or Leu"

:

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 98
- (D) OTHER INFORMATION: /note= "Xaa at position 98 is Thr or Gln"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 102
- (D) OTHER INFORMATION: /note= "Xaa at position 102 is Lys, Val, Trp, or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 103
- (D) OTHER INFORMATION: /note= "Xaa at position 103 is Thr or Ser"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 106
- (D) OTHER INFORMATION: /note= "Xaa at position 106 is Asn, Gln, or His"

(ix) FEATURE:

- (A) NAME/KEY: Modified-site
- (B) LOCATION: 109
- (D) OTHER INFORMATION: /note= "Xaa at position 109 is Ala or Glu"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Asn	Cys	Ser	Xaa	Xaa	Xaa	Asp	Glu	Xaa	Ile	Xaa	His	Leu	Lys	Xaa	Pro
1															15

Pro	Xaa	Pro	Xaa	Leu	Asp	Xaa	Xaa	Asn	Leu	Asn	Xaa	Glu	Asp	Xaa	Xaa
															20
															25

Ile	Leu	Xaa	Xaa	Xaa	Asn	Leu	Arg	Xaa	Xaa	Asn	Leu	Xaa	Xaa	Phe	Xaa
															35
															40

Xaa	Ala	Xaa	Lys	Xaa	Leu	Xaa	Asn	Ala	Ser	Xaa	Ile	Glu	Xaa	Ile	Leu
															50
															55

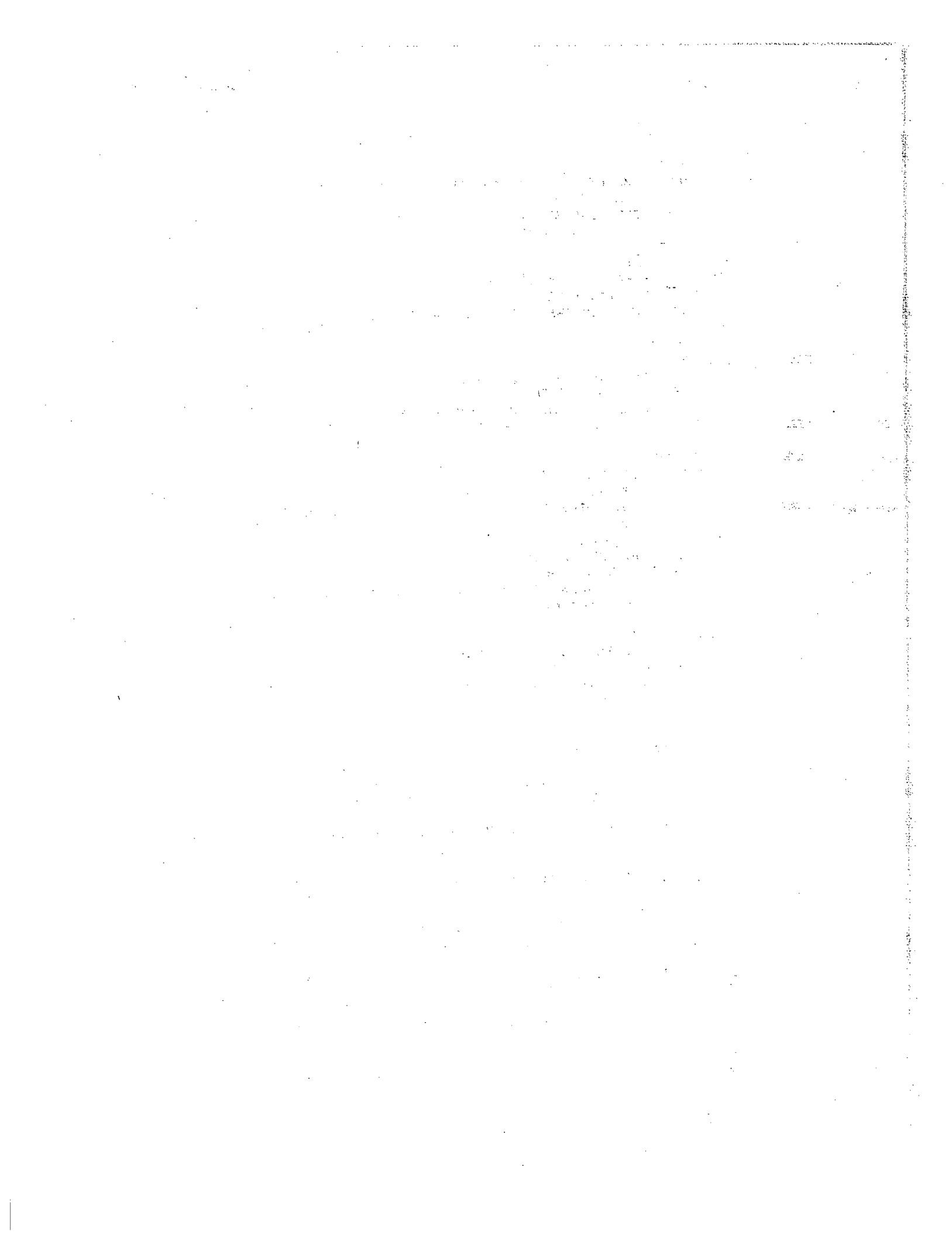
Xaa	Asn	Xaa	Xaa	Pro	Cys	Xaa	Pro	Xaa	Xaa	Thr	Ala	Xaa	Pro	Xaa	Arg
															65
															70

Xaa	Pro	Ile	Xaa	Ile	Xaa	Xaa	Gly	Asp	Trp	Xaa	Glu	Phe	Arg	Xaa	Lys
															85
															90

Leu	Xaa	Phe	Tyr	Leu	Xaa	Xaa	Leu	Glu	Xaa	Ala	Gln	Xaa	Gln	Gln	
															100
															105

110

(2) INFORMATION FOR SEQ ID NO:9:



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85

90

95

Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro
 1 5 10 15

Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp
 20 25 30

Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
 35 40 45

Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu
 50 55 60

Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg
 65 70 75 80

His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys
 85 90 95

Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
 100 105 110

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

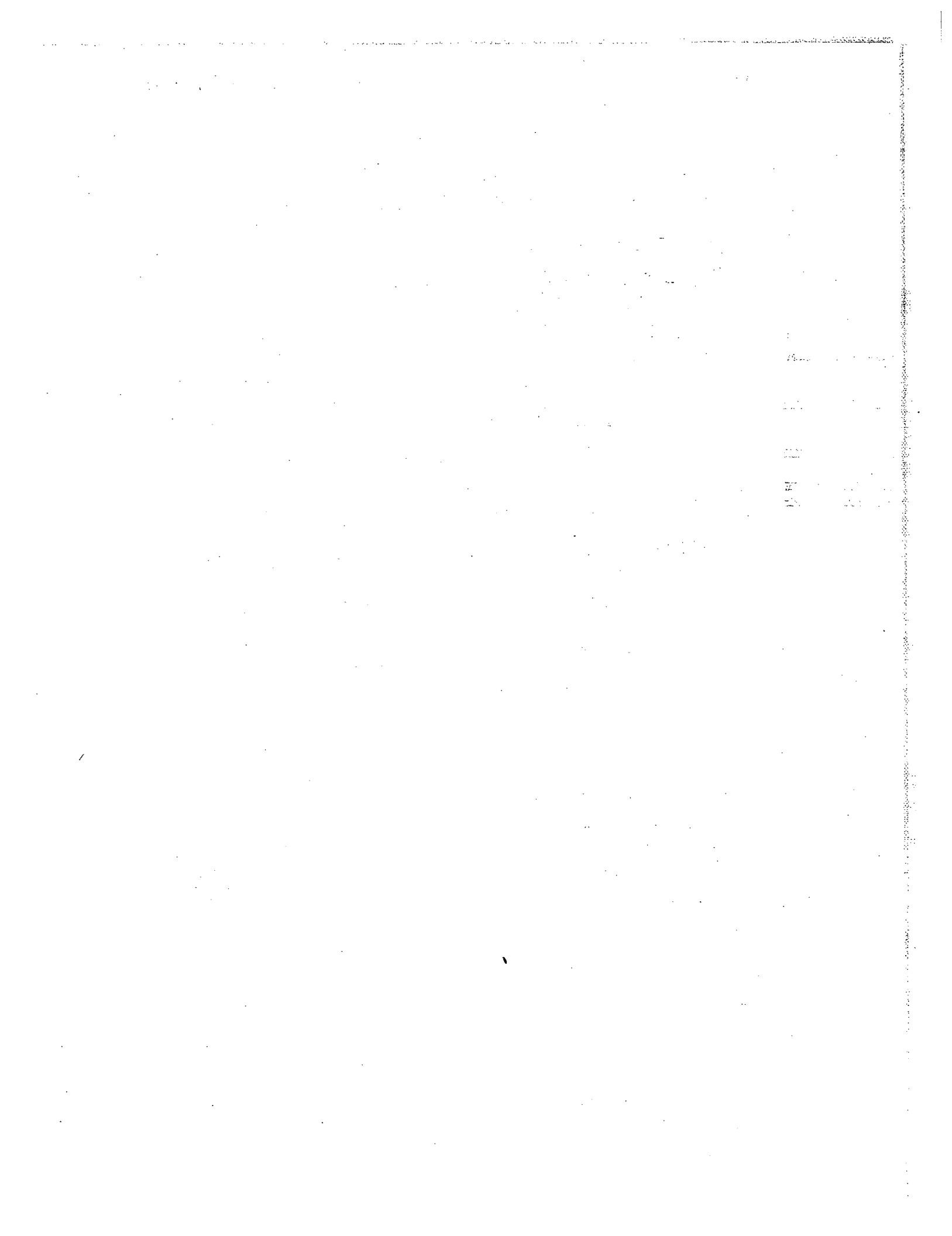
(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro
 1 5 10 15

Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
 20 25 30

Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val
 35 40 45



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Pro	Leu	Pro	Leu	Leu	Asp	Phe	Asn	Asn	Leu	Asn	Gly	Glu	Asp	Gln	Asp
					20				25			30			
Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Thr	Pro	Asn	Leu	Leu	Ala	Phe	Val
					35			40				45			
Arg	Ala	Val	Lys	His	Leu	Glu	Asn	Ala	Ser	Ala	Ile	Glu	Ser	Ile	Leu
					50			55			60				
Lys	Asn	Leu	Leu	Pro	Cys	Leu	Pro	Leu	Ala	Thr	Ala	Ala	Pro	Thr	Arg
					65			70			75			80	
His	Pro	Ile	His	Ile	Lys	Asp	Gly	Asp	Trp	Asn	Glu	Phe	Arg	Arg	Lys
					85			90				95			
Leu	Thr	Phe	Tyr	Leu	Lys	Thr	Leu	Glu	Asn	Ala	Gln	Ala	Gln	Gln	
					100			105			110				

(2) INFORMATION FOR SEQ ID NO:15:

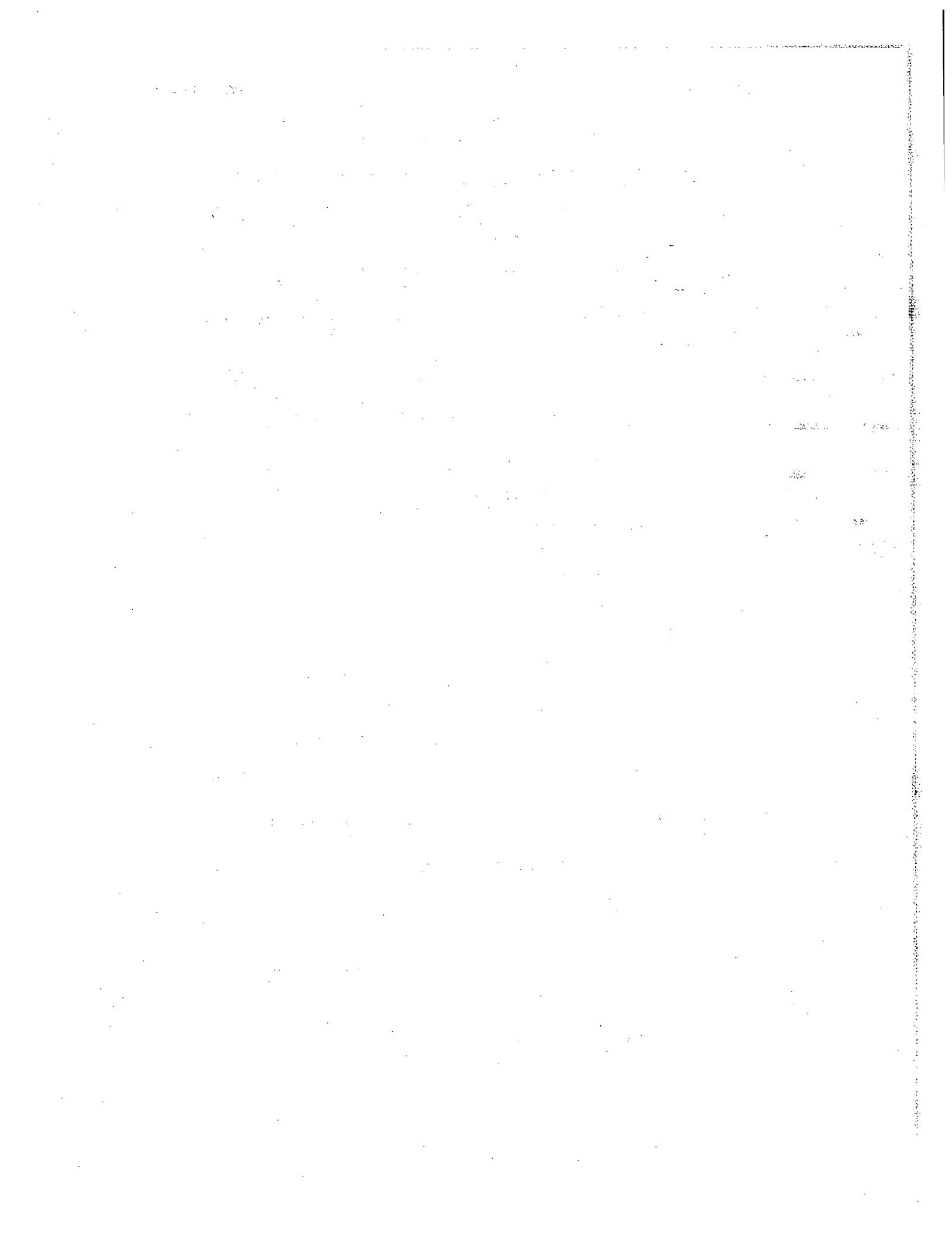
- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 111 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Asn	Cys	Ser	Asn	Met	Ile	Asp	Glu	Ile	Ile	Thr	His	Leu	Lys	Gln	Pro
1					5				10						15
Pro	Leu	Pro	Leu	Leu	Asp	Phe	Asn	Asn	Leu	Asn	Gly	Glu	Asp	Gln	Asp
					20				25				30		
Ile	Leu	Met	Glu	Asn	Asn	Leu	Arg	Arg	Pro	Asn	Leu	Glu	Ala	Phe	Asn
					35			40			45				
Arg	Ala	Val	Lys	Ser	Leu	Gln	Asn	Ala	Ser	Gly	Ile	Glu	Ala	Ile	Leu
					50			55			60				
Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro	Ser	Arg
					65			70			75			80	
His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg	Arg	Lys
					85			90				95			
Leu	Thr	Phe	Tyr	Leu	Lys	Thr	Leu	Glu	Asn	Ala	Gln	Ala	Gln	Gln	
					100			105			110				

(2) INFORMATION FOR SEQ ID NO:16:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 111 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide



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- (A) LENGTH: 111 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Asn	Cys	Ser	Asn	Met	Ile	Asp	Glu	Ile	Ile	Thr	His	Leu	Lys	Gln	Pro
1				5					10					15	

Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
20 25 30

Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
35 40 45

Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu
50 55 60

Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg
65 70 75 80

His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Glu Lys
85 90 95

Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln Gln
100 105 110

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro
1 5 10 15

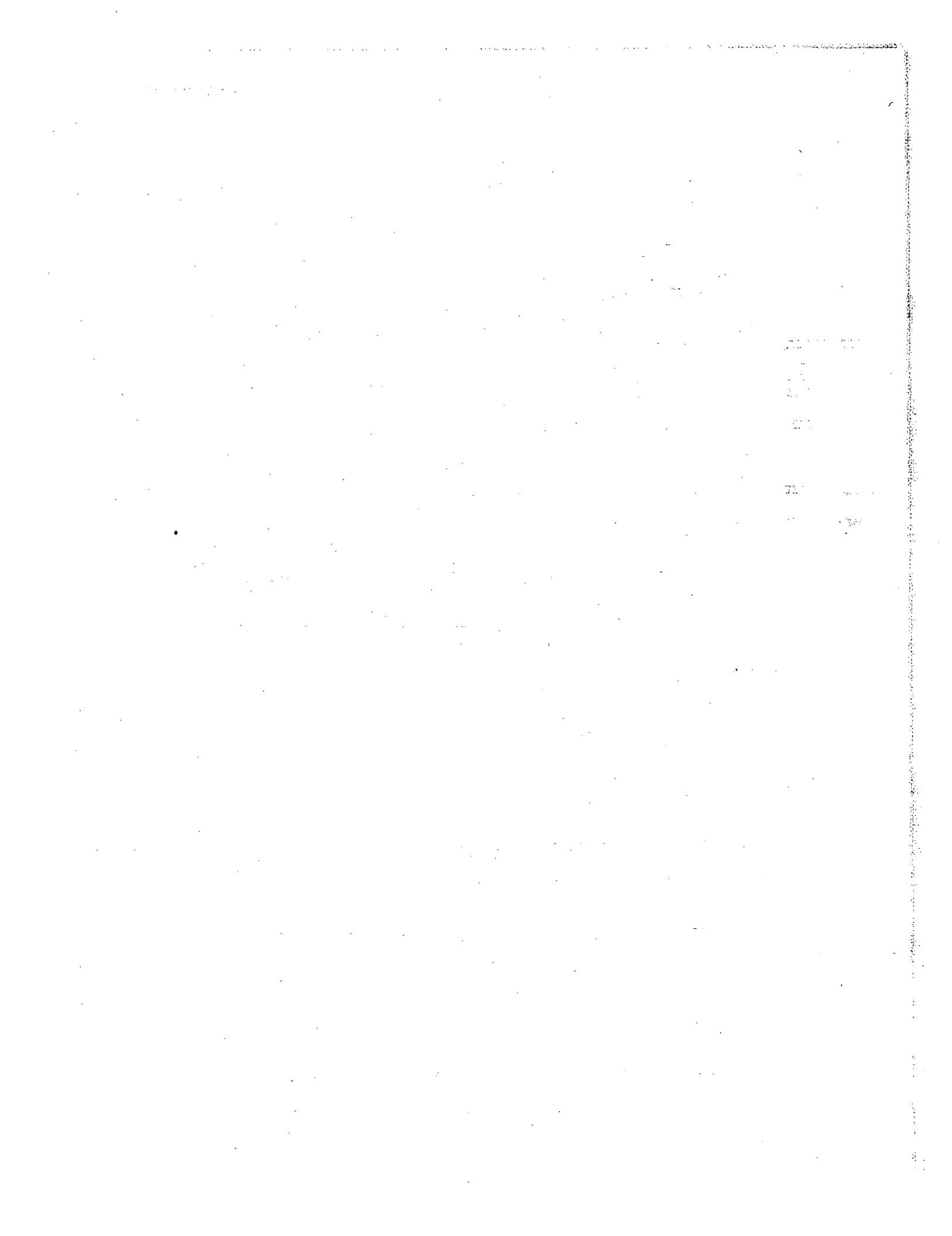
Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp
20 25 30

Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn
35 40 45

Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala Ile Leu
50 55 60

Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg
65 70 75 80

His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys
85 90 95



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Arg	Asn	Leu	Val	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro	Ser	Arg
65									75					80	

His	Pro	Ile	Thr	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg	Glu	Lys
85									90				95		

Leu	Thr	Phe	Tyr	Leu	Val	Ser	Leu	Glu	His	Ala	Gln	Glu	Gln	Gln
100								105				110		

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys	Arg	Pro
1									10				15		

Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ala	Glu	Asp	Val	Asp
20									25				30		

Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Leu	Pro	Asn	Leu	Glu	Ser	Phe	Val
35								40				45			

Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser	Ala	Ile	Glu	Ser	Ile	Leu
50								55				60			

Lys	Asn	Leu	Leu	Pro	Cys	Leu	Pro	Leu	Ala	Thr	Ala	Ala	Pro	Thr	Arg
65								70				75		80	

His	Pro	Ile	His	Ile	Lys	Asp	Gly	Asp	Trp	Asn	Glu	Phe	Arg	Arg	Lys
85								90				95			

Leu	Thr	Phe	Tyr	Leu	Lys	Thr	Leu	Glu	Asn	Ala	Gln	Ala	Gln	Gln
100								105				110		

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

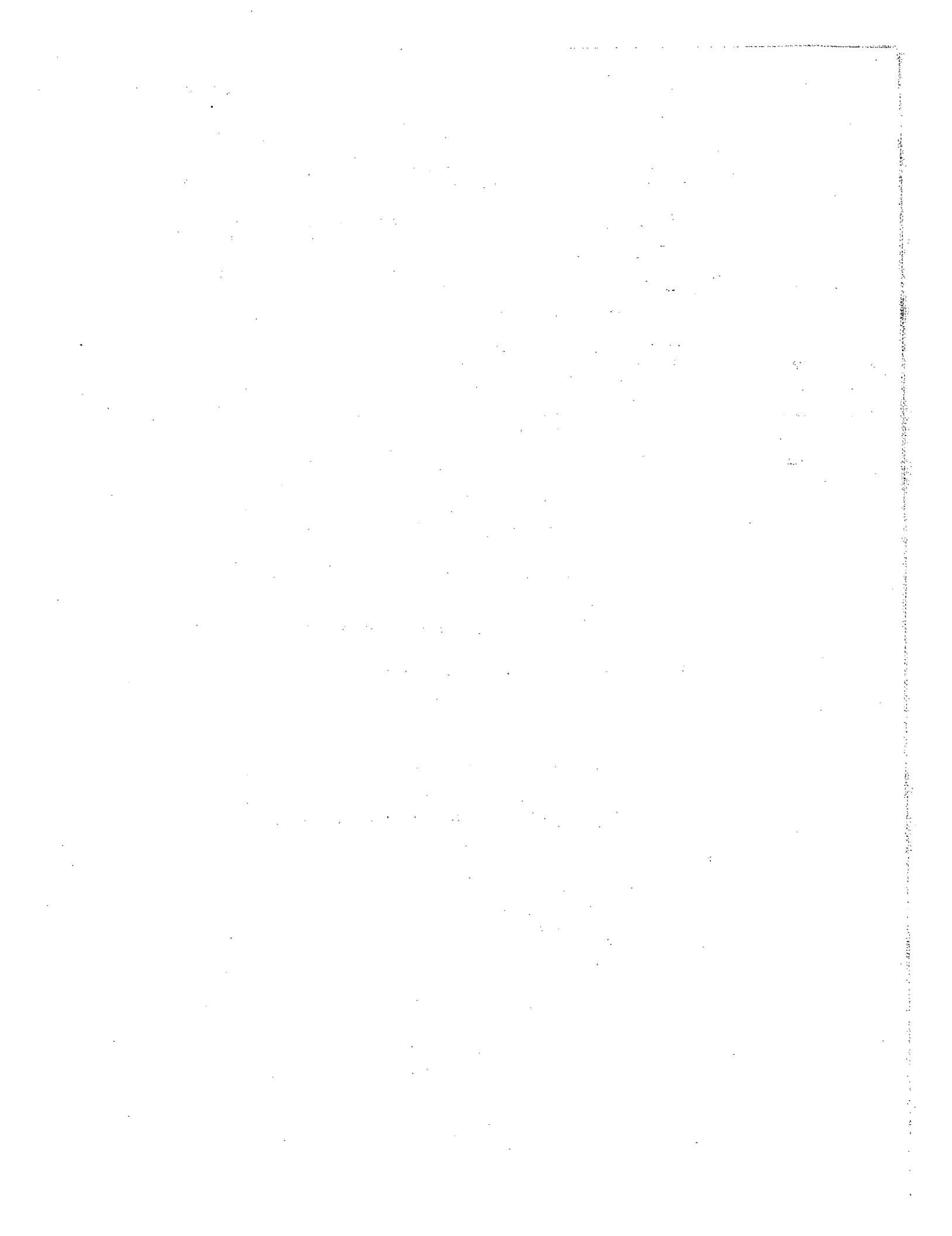
- (A) LENGTH: 111 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys	Arg	Pro
1								5				10		15	

Pro	Asn	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ser	Glu	Asp	Met	Asp
20								25				30			



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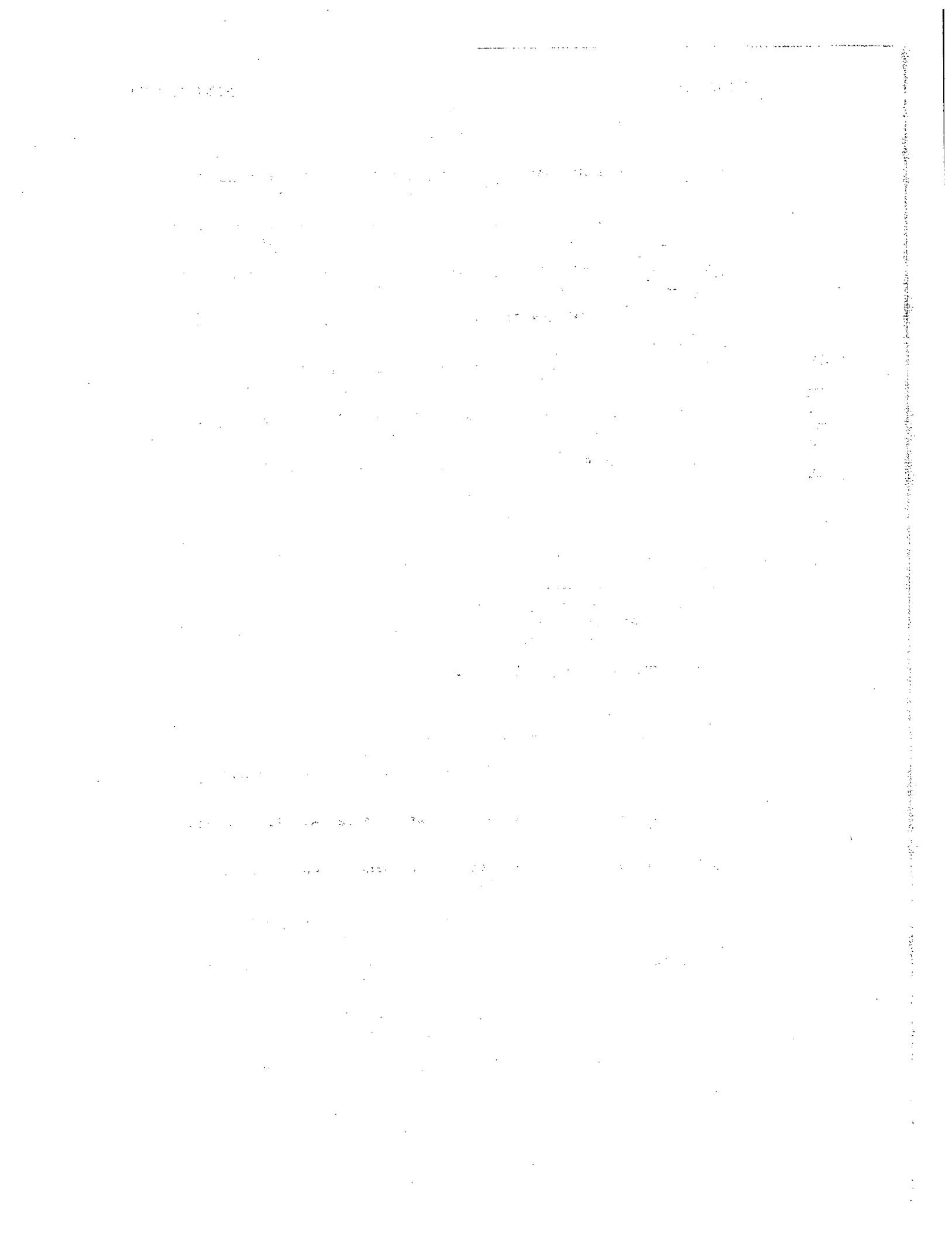
Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys			
1	5	10	15
Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp			
20	25	30	
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala			
35	40	45	
Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90	95	
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100	105	110	
Gln			

(2) INFORMATION FOR SEQ ID NO:26:

- (i) SEQUENCE CHARACTERISTICS:**
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide**

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys			
1	5	10	15
Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp			
20	25	30	
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala			
35	40	45	
Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80
Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90	95	
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100	105	110	
Gln			



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Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro
 65 70 75 80
 Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg
 85 90 95
 Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:29:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

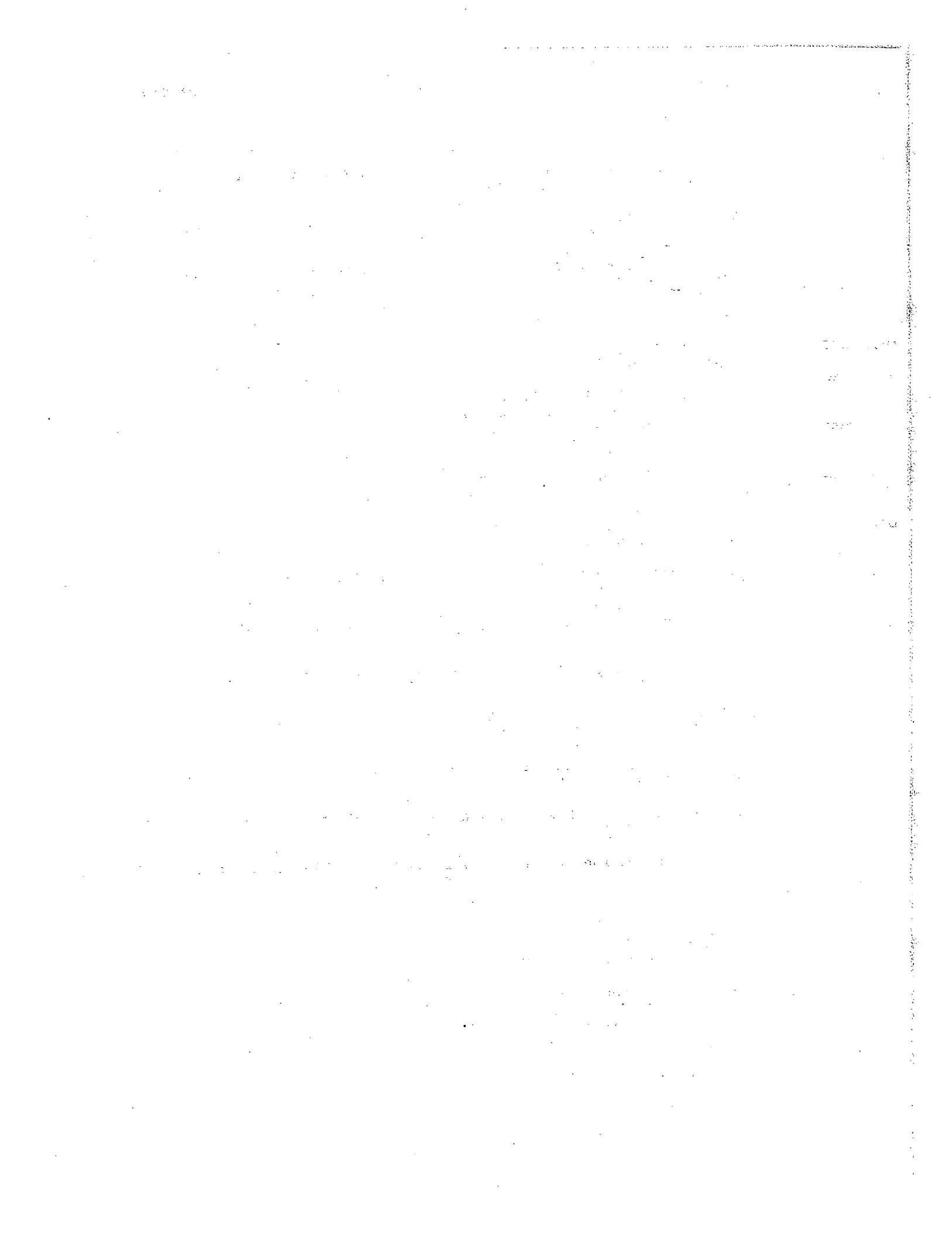
Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Ile Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile Glu Ser
 50 55 60
 Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro
 65 70 75 80
 Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg
 85 90 95
 Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln
 100 105 110
 Gln

(2) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:



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(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

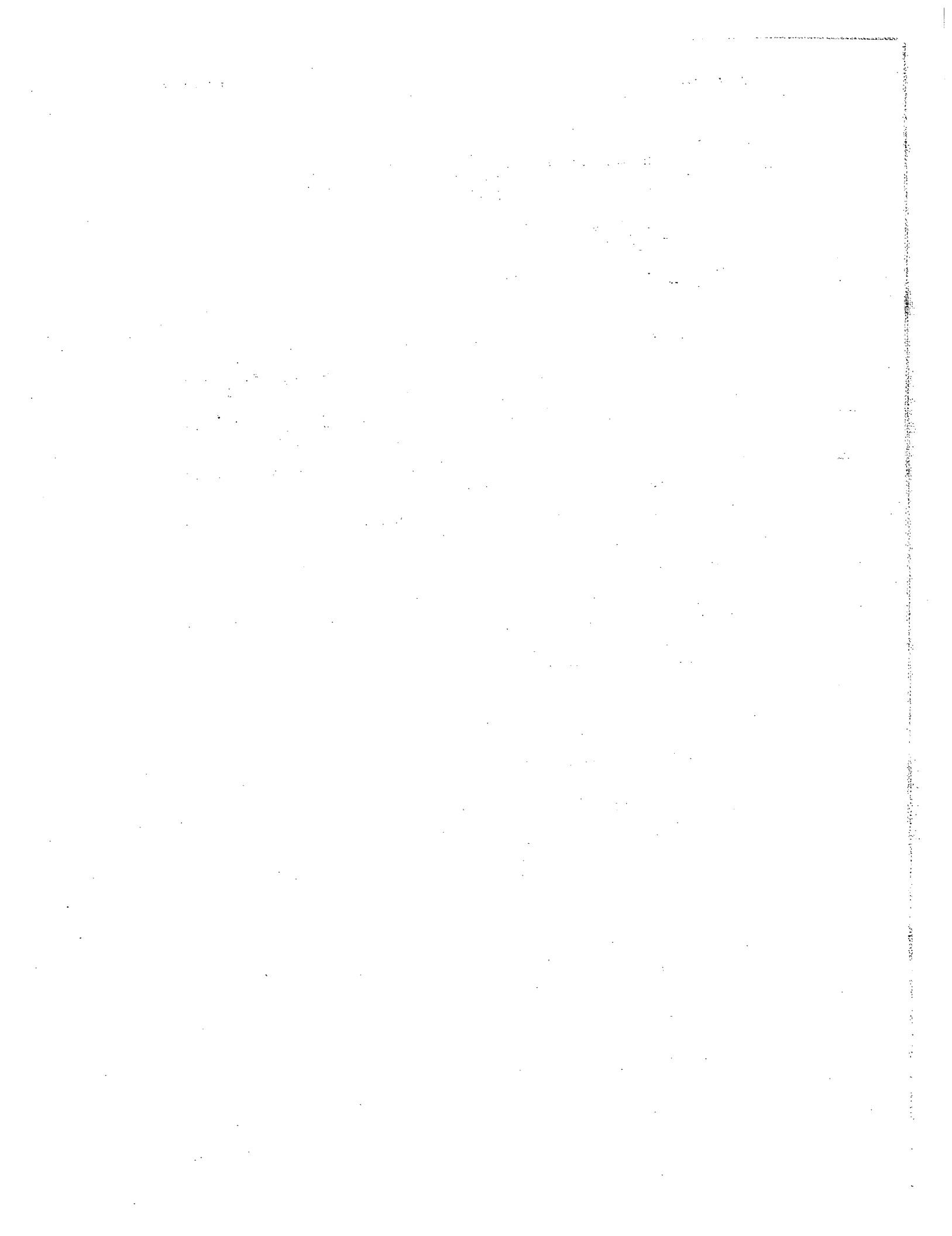
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60



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Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15
Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp			
20	25	30	
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala			
35	40	45	
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80
Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90	95	
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100	105	110	
Gln			

(2) INFORMATION FOR SEQ ID NO:36:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp			
20	25	30	
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala			
35	40	45	
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80
Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90	95	
Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln			
100	105	110	
Gln			

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(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
100 105 110

Gln

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

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Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 . 75 80

Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 .. 95

Glu Lys Leu Thr Phe Tyr .Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp
20 25 30

Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 86 87 88 89 90 91 92 93 94 95

Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu His Ala Gln Glu Gln
100 105 110

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(2) INFORMATION FOR SEO ID NO:40:

(i) SEQUENCE CHARACTERISTICS -

- SEQUENCE CHARACTERISTICS:

 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10.

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Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp			
20	25	30	
Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Ser Asn Leu Glu Ser			
35	40	45	
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80
Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90	95	
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100	105	110	
Gln			

(2) INFORMATION FOR SEQ ID NO:41:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His Leu Lys			
1	5	10	15
Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp			
20	25	30	
Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser			
35	40	45	
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80
Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90	95	
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100	105	110	
Gln			

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(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Lys
1						5				10				15

Arg	Pro	Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Asp	Glu	Asp
					20			25					30		

Met	Ser	Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Leu	Pro	Asn	Leu	Glu	Ser
				35				40					45		

Phe	Val	Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala
				50			55					60			

Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro
				65			70			75				80	

Ser	Arg	His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg
				85			90						95		

Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln	Glu	Gln
				100			105					110			

Gln

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Lys
1						5				10				15

Arg	Pro	Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ala	Glu	Asp
					20			25					30		

Val	Asp	Ile	Leu	Met	Asp	Arg	Asn	Leu	Arg	Leu	Pro	Asn	Leu	Glu	Ser
				35				40					45		

Phe	Val	Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala
				50			55			60					

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Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gin Glu Gln
100 105 110

G1n

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
20 25 30

Val Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

Gln

INFORMATION FOR SEO ID NO:45:

131

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

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Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30

Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln

(2) INFORMATION FOR SEQ ID NO:46:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 125 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys
 1 5 10 15

Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala
 20 25 30

Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu
 35 40 45

Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala
 50 55 60

Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
 65 70 75 80

Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
 85 90 95

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
 100 105 110

Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 115 120 125

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(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 125 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn Cys
1 5 10 15

Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn
20 25 30

Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
35 40 45

Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
50 55 60

Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
65 70 75 80

Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
85 90 95

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
100 105 110

Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
115 120 125

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 113 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His Leu Lys
1 5 10 15

Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser Glu Asp
20 25 30

Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

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Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro
65					70					75					80
Ser	Arg	His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg
	85						90							95	
Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln	Glu	Gln
				100			105						110		
Gln															

(2) INFORMATION FOR SEQ ID NO:49:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 134 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Met	Ala	Pro	Met	Thr	Gln	Thr	Thr	Ser	Leu	Lys	Thr	Ser	Trp	Val	Asn
1				5					10					15	

Cys	Ser	Asn	Met	Ile	Asp	Glu	Ile	Ile	Thr	His	Leu	Lys	Gln	Pro	Pro
			20					25						30	

Leu	Pro	Leu	Leu	Asp	Phe	Asn	Asn	Leu	Asn	Gly	Glu	Asp	Gln	Asp	Ile
				35			40							45	

Leu	Met	Glu	Asn	Asn	Leu	Arg	Arg	Pro	Asn	Leu	Glu	Ala	Phe	Asn	Arg
	50				55				60						

Ala	Val	Lys	Ser	Leu	Gln	Asn	Ala	Ser	Ala	Ile	Glu	Ser	Ile	Leu	Lys
65					70					75				80	

Asn	Leu	Leu	Pro	Cys	Leu	Pro	Leu	Ala	Thr	Ala	Ala	Pro	Thr	Arg	His
			85					90					95		

Pro	Ile	His	Ile	Lys	Asp	Gly	Asp	Trp	Asn	Glu	Phe	Arg	Arg	Lys	Leu
			100					105					110		

Thr	Phe	Tyr	Leu	Lys	Thr	Leu	Glu	Asn	Ala	Gln	Ala	Gln	Gln	Thr	Thr
			115				120						125		

Leu	Ser	Leu	Ala	Ile	Phe
			130		

(2) INFORMATION FOR SEQ ID NO:50:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 36 amino acids
 - (B) TYPE: amino acid

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Gly Gly Gly Ser Gly Gly Ser Gly Gly Ser Glu Gly Gly Gly
1 5 10 15

Ser Glu Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser
20 25 30

Gly Gly Gly Ser
35

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Ile Ser Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro
1 5 10 15

Ser Lys Glu Ser His Lys Ser Pro
20

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 28 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Ile Glu Gly Arg Ile Ser Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
1 5 10 15

Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 906 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGGGCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGGGGCTCC AACATGGCTA CACCATTAGG CCCTGCCAGC	420
TCCCTGCCCG AGAGCTTCCT GCTCAAGTGC TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT	480
GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG	540
GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGGCCAG	600
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTCTCT CTACCAGGGG	660
CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGTC CCACCTTGGA CACACTGCAG	720
CTGGACGTCG CCGACTTGC CACCACCATC TAACTGGAA TGGCCCTGCT CCTGCAGCCC	780
ACCCAGGGTG CCATGCCGGC CTTCGCCTCT GCTTCCAGC GCCGGGCAGG AGGGGTCTG	840
GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGC	900
CAGCCC	906

(2). INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180

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GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT	420
GAAATTATAAC ATCACTTAAA GAGACCACCT AACCCCTTGC TGGACCCGAA CAACCTCAAT	480
TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTG	540
GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC	600
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA	660
GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC TGGTTACCCCT TGAGCAAGCG	720
CAGGAACAAAC AG	732

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCAC CGGCTCGTTC CCCGTCCCCG	420
TCTACCCAGC CGTGGGAACA CGTGAATGCC ATCCAGGAGG CCCGGCGTCT CCTGAACCTG	480
AGTAGAGACA CTGCTGCTGA GATGAATGAA ACAGTAGAAG TGATATCAGA AATGTTGAC	540
CTCCAGGAGC CGACTTGCCT ACAGACCCGC CTGGAGCTGT ACAAGCAGGG CCTGCGGGGC	600
AGCCTCACCA AGCTCAAGGG CCCCTTGACC ATGATGGCCA GCCACTACAA GCAGCACTGC	660
CCTCCAACCC CGGAAACTTC CTGTGCAACC CAGATTATCA CCTTTGAAAG TTTCAAAGAG	720
AACCTGAAGG ACTTCCTGCT TGTCACTCCCC TTTGACTGCT GGGAGCCAGT CCAGGAG	777

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(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC	420
TCCCTGCCCG AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT	480
GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG	540
GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG	600
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTCCCT CTACCAGGGG	660
CTCCTGCAGG CCCTGGAAGG GATATCCCCC GAGTTGGTC CCACCTTGGG CACACTGCAG	720
CTGGACGTG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAAGAACT GGGAAATGGCC	780
CCTGCCCTGC AGCCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG	840
GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT	900
CTACGCCACC TTGCGCAGCC C	921

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 951 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

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ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTC CAGTACCACC AGGTGAAGAT	420
TCCAAAGATG TGGCCGCCCC ACACAGACAG CCACTCACCT CTTCAGAACG AATTGACAAA	480
CAAATTGGT ACATCCTCGA CGGGATATCA GCCCTGAGAA AGGAGACATG TAACAAGAGT	540
AACATGTGTG AAAGCAGCAA AGAGGCCTA GCAGAAAACA ACCTGAACCT TCCAAAGATG	600
GCTGAAAAAG ATGGATGCTT CCAATCCGGA TTCAATGAGG AGACTTGCTT GGTGAAAATC	660
ATCACTGGTC TTTGGAGTT TGAGGTATAC CTCGAGTACC TCCAGAACAG ATTTGAGAGT	720
AGTGAGGAAC AAGCCAGAGC TGTGCAGATG TCGACAAAAG TCCTGATCCA GTTCCTGCAG	780
AAAAAGGCAA AGAATCTAGA TGCAATAACC ACCCCTGACC CAACCACAAA TGCATCCCTG	840
CTGACGAAGC TCCAGGCACA GAACCAGTGG CTGCAGGACA TGACAACCTCA TCTCATTCTG	900
CGCAGCTTTA AGGAGTTCCCT GCAGTCCAGC CTGAGGGCTC TTCGGCAAAT G	951

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTCGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT	420

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GAAATTATAAC ATCACTTAAA GAGACCACCT AACCCCTTGCG TGGACCCGAA CAACCTCAAT 480
 TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTG 540
 GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC 600
 CAACCATGTC TGCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA 660
 GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC TGGTTACCCCT TGAGCAAGCG 720
 CAGGAACAAAC AG 732

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC 60
 CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC 120
 CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA 180
 GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC 240
 TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG 300
 TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGATT 360
 TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC 420
 TCCCTGCCCG AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT 480
 GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG 540
 GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG 600
 GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTCT CTACCAGGGG 660
 CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGTC CCACCTTGGG CACACTGCAG 720
 CTGGACGTGCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAAGAACT GGGAAATGGCC 780
 CCTGCCCTGC AGCCCACCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG 840
 GCAGGAGGGG TCCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT 900
 CTACGCCACC TTGCGCAGCC C 921

(2) INFORMATION FOR SEQ ID NO:60:

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- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC	420
TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT	480
GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG	540
GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGGCCAG	600
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTCT CTACCAGGGG	660
CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGTC CCACCTTGGA CACACTGCAG	720
CTGGACGTCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAAGAACT GGGATGGCC	780
CCTGCCCTGC AGCCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG	840
GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT	900
CTACGCCACC TTGGCGAGCC C	921

- (2) INFORMATION FOR SEQ ID NO:61:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 732 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
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60

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CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG GTGGTTCTGG CGGGGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT	420
GAAATTATAAC ATCACTTAAA GAGACCACCT AACCCCTTGC TGGACCCGAA CAACCTCAAT	480
TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTC	540
GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC	600
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA	660
GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC TGGTTACCCCT TGAGCAAGCG	720
CAGGAACAAAC AG	732

(2) INFORMATION FOR SEQ ID NO:62:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 777 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC	480
TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAAACC TCAATTCTGA AGACATGGAT	540
ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG	600
CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCC	660

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TCTGCCACGG CCCCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA	720
TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG	777

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC	480
TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAAACC TCAATTCTGA AGACATGGAT	540
ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG	600
CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTCGTA ATCTCCAACC ATGTCTGCC	660
TCTGCCACGG CCCCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA	720
TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG	777

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
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CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCCTC GTCTAAAGAA	420
TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC	480
TTAAAGAGAC CACCTAACCC TTTGCTGGAC CCGAACAAACC TCAATTCTGA AGACATGGAT	540
ATCCTGATGG AACGAAACCT TCGAACTCCA AACCTGCTCG CATTGTAAG GGCTGTCAAG	600
CACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCCAACC ATGTCTGCC	660
TCTGCCACGG CCCCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA	720
TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG	777

(2) INFORMATION FOR SEQ ID NO:65:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1047 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAGGATT	360
TCCCCGGGC CTCTGTCAA TGCTGGCGGC GGCTCTGGTG GTGGTTCTGG TGGCGGCTCT	420
GAGGGTGGCG GCTCTGAGGG TGGCGGTTCT GAGGGTGGCG GCTCTGAGGG TGGCGGTTCC	480
GGTGGCGGCT CCGGTTCCGG TGATTTGAT TATGAAAACA TGGCTACACC ATTGGGCCCT	540
GCCAGCTCCC TGCCCCAGAG CTTCCTGCTC AAGTCTTTAG AGCAAGTGAG GAAGATCCAG	600
GGCGATGGCG CAGCGCTCCA GGAGAAGCTG TGTGCCACCT ACAAGCTGTG CCACCCCGAG	660

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GAGCTGGTGC TGCTCGGACA CTCTCTGGGC ATCCCCTGGG CTCCCCTGAG CTCCTGCC	720
AGCCAGGGCC TGCAGCTGGC AGGCTGCTTG AGCCAACCTCC ATAGCGGCCT TTTCCCTCTAC	780
CAGGGGCTCC TGCAGGGCCCT GGAAGGGATA TCCCCGAGT TGGGTCCCAC CTTGGACACA	840
CTGCAGCTGG ACCTCGCCGA CTTTGCCACC ACCATCTGGC ACCAGATGGA AGAACTGGGA	900
ATGGCCCTTG CCCTGCAGCC CACCCAGGGT GCCATGCCGG CCTTCGCCTC TGCTTCCAG	960
CGCCGGGCAG GAGGGGTCT GGTTGCTAGC CATTCGAGA GCTTCCTGGA GGTGTCGTAC	1020
CGCGTTCTAC GCCACCTTGC GCAGCCC	1047

(2) INFORMATION FOR SEQ ID NO:66:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 903 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACCTAATCGA GGGAAAGGATT	360
TCCCCCGGGC CTCCGTCAA TGCTGGGGC GGCTCTGGTG GTGGTTCTGG TGGGGCTCT	420
GAGGGTGGCG GCTCTGAGGG TGGCGGTTCT GAGGGTGGCG GCTCTGAGGG TGGCGGTTCC	480
GGTGGCGGCT CCCGTTCCGG TGATTTGAT TATGAAAACA TGGCACCGGC TCGTTCCCCG	540
TCCCCGTCTA CCCAGCCGTG GGAACACCGTG AATGCCATCC AGGAGGCCCG GCGTCTCCTG	600
AACCTGAGTA GAGACACTGC TGCTGAGATG AATGAAACAG TAGAAGTGAT ATCAGAAATG	660
TTTGACCTCC AGGAGCCGAC TTGCTACAG ACCGGCCTGG AGCTGTACAA GCAGGGCCTG	720
CGGGGCAGCC TCACCAAGCT CAAGGGCCCC TTGACCATGA TGGCCAGCCA CTACAAGCAG	780
CACTGCCCTC CAACCCCGGA AACCTCCGT GCAACCCAGA TTATCACCTT TGAAAGTTTC	840
AAAGAGAACCC TGAAGGACTT CCTGCTTGTC ATCCCTTTG ACTGCTGGGA GCCAGTCCAG	900
GAG	903

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(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1017 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCCGGTG GC GGCGCTC TGGTGGTGGT TCTGGTGGCG GCTCTGAGGG TGGCGGCTCT	420
GAGGGTGGCG GTTCTGAGGG TGGCGGCTCT GAGGGTGGCG GTTCCGGTGG CGGCTCCGGT	480
TCCGGTAACA TGGCTACACC ATTAGGCCCT GCCAGCTCCC TGCCCCAGAG CTTCTGCTC	540
AAGTGCTTAG AGCAAGTGAG GAAGATCCAG GGCGATGGCG CAGCGCTCCA GGAGAAGCTG	600
TGTGCCACCT ACAAGCTGTG CCACCCCGAG GAGCTGGTGC TGCTCGGACA CTCTCTGGC	660
ATCCCCCTGGG CTCCCCTGAG CTCTGCCCT AGCCAGGCC TGCA GCTGGC AGGCTGCTTG	720
AGCCAACCTCC ATAGCGGCCT TTTCTCTAC CAGGGGCTCC TGCAGGCCCT GGAAGGGATA	780
TCCCCCGAGT TGGGTCCCAC CTTGGACACA CTGCAGCTGG ACGTCGCCGA CTTTGCCACC	840
ACCATCTGGC AGCAGATGGA AGAACTGGGA ATGGCCCTG CCCTGCAGCC CACCCAGGGT	900
GCCATGCCGG CCTCGCCTC TGCTTTCCAG CGCCGGCAG GAGGGGTCCCT GGTTGCTAGC	960
CATCTGCAGA GCTTCTGGA GGTGTCGTAC CGCGTTCTAC GCCACCTTGC GCAGCCC	1017

(2). INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

ATGGCTAAGT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCAGCTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAAT CTCCAAACAT GGCTACACCA TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC	480
TTCCCTGCTCA AGTGCTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG	540
GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTGGACAC	600
TCTCTGGCA TCCCCTGGC TCCCCTGAGC TCCTGCCCA GCCAGGCCCT GCAGCTGGCA	660
GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG	720
GAAGGGATAT CCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC	780
TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGAA TGGCCCTGCG CCTGCAGCCC	840
ACCCAGGGTG CCATGCCGGC CTTGCCCTCT GCTTCCAGC GCCGGGCAGG AGGGGCTCTG	900
GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG	960
CAGCCC	966

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 822 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

ATGGCTAAGT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCAGCTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300

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TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAT CTCCAAACAT GGCACCGGCT CGTTCCCCGT CCCCCTCTAC CCAGCCGTGG	480
GAACACCGTGA ATGCCATCCA GGAGGCCGG CGTCTCCTGA ACCTGAGTAG AGACACTGCT	540
GCTGAGATGA ATGAAACAGT AGAAAGTGATA TCAGAAATGT TTGACCTCCA GGAGCCGACT	600
TGCTTACAGA CCCGCCTGGA GCTGTACAAG CAGGGCCTGC GGGGCAGCCT CACCAAGCTC	660
AAGGGCCCT TGACCATGAT GGCCAGCCAC TACAAGCAGC ACTGCCCTCC AACCCCGGAA	720
ACTTCCGTG CAACCCAGAT TATCACCTT GAAAGTTCA AAGAGAACCT GAAGGACTTC	780
CTGCTTGTCA TCCCCTTGA CTGCTGGAG CCAGTCCAGG AG	822

(2) INFORMATION FOR SEQ ID NO: 70:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 966 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAT CTCCAAACAT GGCTACACCA TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC	480
TTCCCTGCTCA AGTGCTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG	540
GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTGGACAC	600
TCTCTGGGCA TCCCCTGGC TCCCCTGAGC TCCTGCCCA GCCAGGCCCT GCAGCTGGCA	660
GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCCTCTACC AGGGGCTCCT GCAGGCCCTG	720
GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC	780
TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGAA TGGCCCTGC CCTGCAGCCC	840

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ACCCAGGGTG CCATGCCGGC CTTGCCTCT GCTTCCAGC GCCGGCAGG AGGGTCCTG	900
GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGCGTACCG CGTCTACG CCACCTTGC	960
CAGCCC	966

(2) INFORMATION FOR SEQ ID NO:71:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 966 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGGCCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCCTC GTCTAAAGAA	420
TCTCATAAAAT CTCCAAACAT GGCTACACCA TTAGGCCCTG CCAGCTCCCT GCCCCAGAGC	480
TTCCCTGCTCA AGTGCTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG	540
GAGAACGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGT GCTCGGACAC	600
TCTCTGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCA GCCAGGCCCT GCAGCTGGCA	660
GGCTGCTTGA GCCAACTCCA TAGCGGCCCTT TTCTCTACCC AGGGGCTCCCT GCAGGCCCTG	720
GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC	780
TTTGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGAA TGGCCCTGC CCTGCAGCCC	840
ACCCAGGGTG CCATGCCGGC CTTGCCTCT GCTTCCAGC GCCGGCAGG AGGGTCCTG	900
GTTGCTAGCC ATCTGCAGAG CTTCTGGAG GTGCGTACCG CGTCTACG CCACCTTGC	960
CAGCCC	966

(2) INFORMATION FOR SEQ ID NO:72:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

ATGGCTACAC CATTAGGCC	TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAAGCT GTGTGCCACC	120	
TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCTGG	180	
GCTCCCTGA GCTCCTGCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240	
CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCCGAG	300	
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTGCGCG ACTTTGCCAC CACCATCTGG	360	
CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420	
GCCTTCGCCT CTGCTTCCA GCGCCGGGCA GGAGGGTCC TGGTTGCTAG CCATCTGCAG	480	
AGCTTCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG	540	
GGAAGGATTT CCCCGGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA	600	
ATGATCGATG AAATTATACA TCACTAAAG AGACCACCTA ACCCTTGCT GGACCCGAAC	660	
AACCTCAATT CTGAAGACAT GGATATCCTG ATGGAACGAA ACCTTCGAAC TCCAAACCTG	720	
CTCGCATTCTG TAAGGGCTGT CAAGCACTTA GAAAATGCAT CAGGTATTGA GGCAATTCTT	780	
CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC	840	
ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAAACTGA CGTTCTATCT GGTTACCCCTT	900	
*GAGCAAGCGC AGGAACAAACA G	921	

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

ATGGCTACAC CATTAGGCC	TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAAGCT GTGTGCCACC	120	
TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCTGG	180	

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GCTCCCTGA	GCTCCTGCC	CAGCCAGGCC	CTGCAGCTGG	CAGGCTGCTT	GAGCCAACTC	240
CATAGCGGCC	TTTCCTCTA	CCAGGGCTC	CTGCAGGCC	TGGAAGGGAT	ATCCCCGAG	300
TTGGGTCCA	CCTTGGACAC	ACTGCAGCTG	GACGTCGCCG	ACTTGCCAC	CACCATCTGG	360
CAGCAGATGG	AAGAACTGGG	AATGGCCCCT	GCCCTGCAGC	CCACCCAGGG	TGCCATGCCG	420
GCCTTCGCCT	CTGCTTCCA	GCGCCGGCA	GGAGGGTCC	TGGTTGCTAG	CCATCTGCAG	480
AGCTTCTGG	AGGTGTCGTA	CCGCGTTCTA	CGCCACCTTG	CGCAGCCCTA	CGTAATCGAG	540
GGAAGGATT	CCCCGGGTGA	ACCGTCTGGT	CCAATCTCTA	CTATCAACCC	GTCTCCTCCG	600
TCTAAAGAAT	CTCATAAATC	TCCAAACATG	GCTAACTGCT	CTATAATGAT	CGATGAAATT	660
ATACATCACT	TAAAGAGACC	ACCTAACCTT	TTGCTGGACC	CGAACAAACCT	CAATTCTGAA	720
GACATGGATA	TCCTGATGGA	ACGAAACCTT	CGAACTCCAA	ACCTGCTCGC	ATTGTAAGG	780
GCTGTCAAGC	ACTTAGAAAA	TGCATCAGGT	ATTGAGGCAA	TTCTCGTAA	TCTCCAACCA	840
TGTCTGCCCT	CTGCCACGGC	CGCACCCCTCT	CGACATCCAA	TCATCATCAA	GGCAGGTGAC	900
TGGCAAGAAT	TCCGGGAAAA	ACTGACGTTTC	TATCTGGTTA	CCCTTGAGCA	AGCGCAGGAA	960
CAACAG						966

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1047 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

ATGGCTACAC	CATTAGGCC	TGCCAGCTCC	CTGCCCCAGA	GCTTCCTGCT	CAAGTGCTTA	60
GAGCAAGTGA	GGAAGATCCA	GGCGATGGC	GCAGCGCTCC	AGGAGAAGCT	GTGTGCCACC	120
TACAAGCTGT	GCCACCCCGA	GGAGCTGGTG	CTGCTGGAC	ACTCTCTGGG	CATCCCCCTGG	180
GCTCCCTGA	GCTCCTGCC	CAGCCAGGCC	CTGCAGCTGG	CAGGCTGCTT	GAGCCAACTC	240
CATAGCGGCC	TTTCCTCTA	CCAGGGCTC	CTGCAGGCC	TGGAAGGGAT	ATCCCCGAG	300
TTGGGTCCA	CCTTGGACAC	ACTGCAGCTG	GACGTCGCCG	ACTTGCCAC	CACCATCTGG	360
CAGCAGATGG	AAGAACTGGG	AATGGCCCCT	GCCCTGCAGC	CCACCCAGGG	TGCCATGCCG	420
GCCTTCGCCT	CTGCTTCCA	GCGCCGGCA	GGAGGGTCC	TGGTTGCTAG	CCATCTGCAG	480
AGCTTCTGG	AGGTGTCGTA	CCGCGTTCTA	CGCCACCTTG	CGCAGCCCTA	CGTAATCGAG	540

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GGAAGGATTT	CCCCCGGGCC	TCCTGTCAAT	GCTGGCGGCG	GCTCTGGTGG	TGGTTCTGGT	600
GGCGGGCTCTG	AGGGTGGCGG	CTCTGAGGGT	GGCGGTTCTG	AGGGTGGCGG	CTCTGAGGGT	660
GGCGGGTTCCG	GTGGCGGCTC	CGGTTCCGGT	GATTTTGATT	ATGAAAACAT	GGCTAACTGC	720
TCTATAATGA	TCGATGAAAT	TATACATCAC	TTAAAGAGAC	CACCTAACCC	TTTGCTGGAC	780
CCGAACAACC	TCAATTCTGA	AGACATGGAT	ATCCTGATGG	AACGAAACCT	TCGAACTCCA	840
AACCTGCTCG	CATTCTGTAAG	GGCTGTCAAG	CACTTAGAAA	ATGCATCAGG	TATTGAGGCA	900
ATTCTTCGTA	ATCTCCAACC	ATGTCTGCC	TCTGCCACGG	CCGCACCCCTC	TCGACATCCA	960
ATCATCATCA	AGGCAGGTGA	CTGGCAAGAA	TTCCGGGAAA	AACTGACGTT	CTATCTGGTT	1020
ACCCCTTGAGC	AAGCGCAGGA	ACAAACAG				1047

(2) INFORMATION FOR SEQ ID NO:75:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

ATGGCTACAC	CATTAGGCC	TGCCAGCTCC	CTGCC	CCAGA	GCTTC	CCTGCT	CAAGTGCTTA	60
GAGCAAGTGA	GGAAAGATCCA	GGCGATGGC	GCAGCGCTCC	AGGAGAAGCT	GTGTGCCACC			120
TACAAGCTGT	GCCACCCC	GA	GGAGCTGGTG	CTGCTGGAC	ACTCTCTGGG	CATCCCCTGG		180
GCTCC	CTGA	GCTC	CTGCC	AGCCAGGCC	CTGCAGCTGG	CAGGCTGCTT	GAGCCA	240
CATAGCGGCC	TTTC	CCTCTA	CCAGGGCTC	CTGCAGGCC	TGGAAGGGAT	ATCCCCGAG		300
TGGGT	CCCA	CCTTGGACAC	ACTGCAGCTG	GACGTCGCC	ACTTTGCCAC	CACCATCTGG		360
CAGCAGATGG	AAGAACTGGG	AATGGCC	CTA	CCACCCAGGG	TGCCATGCC			420
GCCTTC	GCCT	CTGCTTCCA	GCGCCGGCA	GGAGGGTCC	TGGTTGCTAG	CCATCTGCAG		480
AGCTT	CCTGG	AGGTGTCGTA	CCGC	GTTCTA	CGCCACCTTG	CGCAGCC	CTAATCGAG	540
GGAAGGATTT	CCCCGGGTGG	TGGTTCTGGC	GGCGG	CTCCA	ACATGGCTAA	CTGCT	CTATA	600
ATGATCGATG	AAATTATA	ACA	TTAAAG	AGACCAC	CTG	CACCTT	GCT GGACCCGAAC	660
AACCTCAATG	ACGAAGACGT	CTCTATCCTG	ATGGAACGAA	ACCTTCGACT	TCC	AAAC	CTG	720
GAGAGCTTCG	TAAGGGCTGT	CAAGAACTTA	GAAATGCAT	CAGGTATTGA	GGCAATT	CTT		780
CGTAATCTCC	AACC	ATGTCT	GCC	CTGCC	ACGGCCGCAC	CCTCTGAC	A	840

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ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAAACTGA CGTTCTATCT GGTTACCCCTT 900
 GAGCAAGCGC AGGAACAACA G 921

(2) INFORMATION FOR SEQ ID NO:76:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1047 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

ATGGCTACAC CATTAGGCC	TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA	GGCGCATGGC GCAGCGCTCC AGGAGAACGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCCGA	GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG	180
GCTCCCCCTGA GCTCCTGCC	CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTCCCTCTA	CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCGAG	300
TTGGGTCCCA CCTTGGACAC	ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG	360
CAGCAGATGG AAGAACTGGG	AATGGCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTCCA	GCGCCGGGCA GGAGGGTCC TGGTTGCTAG CCATCTGCAG	480
AGCTTCTGG AGGTGTCGTA	CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAATCGAG	540
GGAAGGATTT CCCCCGGGCC	TCCTGTCAAT GCTGGCGCG GCTCTGGTGG TGGTTCTGGT	600
GGCGGCTCTG AGGGTGGCGG	CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG CTCTGAGGGT	660
GGCGGTTCCG GTGGCGGCTC	CGGTTCCGGT GATTTGATT ATGAAAACAT GGCTAACTGC	720
TCTATAATGA TCGATGAAAT	TATACATCAC TTAAAGAGAC CACCTGCACC TTTGCTGGAC	780
CCGAACAAACC TCAATGACGA	AGACGTCTCT ATCCTGATGG AACGAAACCT TCGACTTCCA	840
AACCTGGAGA GCTTCGTAAG	GGCTGTCAAG AACTTAGAAA ATGCATCAGG TATTGAGGCA	900
ATTCTTCGTA ATCTCCAACC	ATGTCTGCC TCTGCCACGG CCGCACCCCTC TCGACATCCA	960
ATCATCATCA AGGCAGGTGA	CTGGCAAGAA TTCCGGAAA AACTGACGTT CTATCTGGTT	1020
ACCCCTTGAGC AAGCGCAGGA	ACAAACAG	1047

(2) INFORMATION FOR SEQ ID NO:77:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 966 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

ATGGCTACAC CATTAGGCC	TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAC	GTGTGCCACC	120
TACAAGCTGT GCCACCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG	CATCCCCTGG	180
GCTCCCTGA GCTCCTGCC	CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAAC	240
CATAGCGGCC TTTTCTCTA CCAGGGGCTC CTGCAGGCC	TGGAAGGGAT ATCCCCCGAG	300
TTGGGTCCC	CCTTGGACAC ACTGCAGCTG GACGTGCGG ACTTTGCCAC CACCATCTGG	360
CAGCAGATGG AAGAACTGGG AATGGCCCT	GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTCCA GCGCCGGCA GGAGGGTCC TGGTTGCTAG CCATCTGCAG	480	
AGCTTCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTG CGCAGCCTA CGTAATCGAG	540	
GGAAGGATT	CCCCGGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG	600
TCTAAAGAAT CTCATAAATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT	660	
ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC CGAACAAACCT CAATGACGAA	720	
GACGTCTCTA TCCTGATGGA ACGAAACCTT CGACTTCAA ACCTGGAGAG CTTCGTAAGG	780	
GCTGTCAAGA ACTTAGAAAA TGCATCAGGT ATTGAGGCAA TTCTTCGAA TCTCCAACCA	840	
TGTCTGCCCT CTGCCACGGC CGCACCCCT CGACATCAA TCATCATCAA GGCAGGTGAC	900	
TGGCAAGAAT TCCGGAAAA ACTGACGTTA TATCTGGTTA CCCTTGAGCA AGCCAGGAA	960	
CAACAG		966

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

ATGGCTACAC CATTAGGCC	TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAC	GTGTGCCACC	120

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TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG	180
GCTCCCCCTGA GCTCCTGCCCG CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTCCCTCTA CCAGGGGCTC CTGCAGGCC CGGGCTGCTT GAGCCAACTC	300
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTGCGCG ACTTTGCCAC CACCACATCTGG	360
CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGTTGCTAG CCATCTGCAG	480
AGCTTCCTGG AGGTGTCGTA CGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC	540
GGTGGAGGCT CCCCGGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA	600
ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTGCT GGACCCGAAC	660
AACCTCAATG ACAGAACGACT CTCTATCCTG ATGGAACGAA ACCTTCGACT TCCAAACCTG	720
GAGAGCTTCG TAAGGGCTGT CAAGAACTTA GAAAATGCAT CAGGTATTGA GGCAATTCTT	780
CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC	840
ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAAACTGA CGTTCTATCT GGTTACCCCTT	900
GAGCAAGCGC AGGAACAAACA G	921

(2) INFORMATION FOR SEQ ID NO:79:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 966 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

ATGGCTACAC CATTAGGCC CGGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAAGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG	180
GCTCCCCCTGA GCTCCTGCCCG CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTCCCTCTA CCAGGGGCTC CTGCAGGCC CGGGCTGCTT GAGCCAACTC	300
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTGCGCG ACTTTGCCAC CACCACATCTGG	360
CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA GGAGGGGTCC TGTTGCTAG CCATCTGCAG	480
AGCTTCCTGG AGGTGTCGTA CGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC	540

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GGTGGAGGCT CCCCGGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG	600
TCTAAAGAAC TCTATAAACATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT	660
ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC CGAACAAACCT CAATGACGAA	720
GGACGTCTCTA TCCTGATGGA ACGAAACCTT CGACTTCCAA ACCTGGAGAG CTTCGTAAGG	780
GCTGTCAAGA ACTTAGAAAA TGCAATCAGGT ATTGAGGCAA TTCTTCGTAAC TCTCCAACCA	840
TGTCTGCCCT CTGCCACGGC CGCACCCCTCT CGACATCCAA TCATCATCAA GGCAGGTGAC	900
TGGCAAGAAC TCCGGGAAAA ACTGACGTTT TATCTGGTTA CCCTTGAGCA AGCGCAGGAA	960
GAACAG	966

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 921 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

ATGGCTACAC CATTGGGCC CGCCAGCTCC CTGCCCGAGA GCTTCCTGCT CAAGTCTTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAACGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG	180
GCTCCCTGA GCTCCTGCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTCCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCCGAG	300
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTGCGCG ACTTTGCCAC CACCATCTGG	360
GAGCAGATGG AAGAACTGGG AATGGCCCT GCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG	480
AGCTTCTGG AGGTGTCGTA CGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC	540
GGTGGAGGCT CCCCGGGTGG TGGTTCTGGC GGCGGCTCCA ACATGGCTAA CTGCTCTATA	600
ATGATCGATG AAATTATACA TCACTTAAAG AGACCACCTG CACCTTGCT GGACCCGAAC	660
AACCTCAATG ACGAAGACGT CTCTATCCTG ATGGAACGAA ACCTTCGACT TCCAAACCTG	720
GAGAGCTTCG TAAGGGCTGT CAAGAACTTA GAAAATGCAT CAGGTATTGA GGCAATTCTT	780
CGTAATCTCC AACCATGTCT GCCCTCTGCC ACGGCCGCAC CCTCTCGACA TCCAATCATC	840
ATCAAGGCAG GTGACTGGCA AGAATTCCGG GAAAAACTGA CGTTCTATCT GGTTACCCCTT	900

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GAGCAAGCGC AGGAACAACA G

921

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

ATGGCTACAC CATTGGGCC CGGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTCTTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAAGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCCTGG	180
GCTCCCTGTA GCTCCTGCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCCGAG	300
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG	360
CAGCAGATGG AAGAACTGGG AATGGCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCCT CTGCTTCCA GCGCCGGGCA GGAGGGGTCC TGGTTGCTAG CCATCTGCAG	480
AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTA CGTAGAGGGC	540
GGTGGAGGCT CCCGGGTGA ACCGTCTGGT CCAATCTCTA CTATCAACCC GTCTCCTCCG	600
TCTAAAGAAT CTCATAAACATC TCCAAACATG GCTAACTGCT CTATAATGAT CGATGAAATT	660
ATACATCACT TAAAGAGACC ACCTGCACCT TTGCTGGACC CGAACAAACCT CAATGACGAA	720
GACGTCTCTA TCCTGATGGA ACGAAACCTT CGACTTCAA ACCTGGAGAG CTTCGTAAGG	780
GCTGTCAAGA ACTTAGAAAA TGCATCAGGT ATTGAGGCAA TTCTTCGTAACCA TCTCCAACCA	840
TGTCTGCCCT CTGCCACGGC CGCACCCCTCG ACACATCCAA TCATCATCAA GGCAGGTGAC	900
TGGCAAGAAT TCGGGAAAA ACTGACGTTA TATCTGGTTA CCCTTGAGCA AGCGCAGGAA	960
CAACAG	966

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 777 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGGGCAG GAACAACAGT AC GTAATCGA GGGAGGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC	480
TTAAAGAGAC CACCTGCACC TTTGCTGGAC CCGAACAAACC TCAATGACGA AGACGTCTCT	540
ATCCTGATGG AACGAAACCT TCGACTTCCA AACCTGGAGA GCTTCGTAAG GGCTGTCAAG	600
AACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTCGTA ATCTCCAACC ATGTCTGCC	660
TCTGCCACGG CCCGACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA	720
TTCCGGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG	777

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 984 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGGGCAG GAACAACAGT AC GTAATCGA GGGAGGATT	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAT CTCCAAACAT GGCTACACCA TTGGGCCCTG CCAGCTCCCT GCCCCAGAGC	480

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TTCCTGCTCA AGTCTTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG	540
GAGAACGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTGGACAC	600
TCTCTGGGCA TCCCCTGGGC TCCCCTGAGC TCCTGCCCCA GCCAGGCCCT GCAGCTGGCA	660
GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCCTCTACC AGGGGCTCCT GCAGGCCCTG	720
GAAGGGATAT CCCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC	780
TTCGCCACCA CCATCTGGCA GCAGATGGAA GAACTGGAA TGGCCCTGC CCTGCAGCCC	840
ACCCAGGGTG CCATGCCGGC CTTCGCCTCT GCTTCCAGC GCCGGGCAGG AGGGGTCTG	900
GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG	960
CAGCCCTGAT AAGGATCCGA ATT	984

(2) INFORMATION FOR SEQ ID NO:84:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGGCGCTCC AACATGGCTA CACCATTAGG CCCTGCCAGC	420
TCCCTGCCCT AGAGCTTCCT GCTCAAGTGC TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT	480
GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG	540
GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG	600
GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA CTCCATAGCG GCCTTTCTCT CTACCAGGGG	660
CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGTC CCACCTTGGGA CACACTGCAG	720
CTGGACGTGCG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAGAACT GGGAAATGGCC	780
CCTGCCCTGC AGCCCACCCA GGGTGCCATG CGGGCCTTCG CCTCTGCTTT CCAGCGCCGG	840

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GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT	900
CTACGCCACC TTGCGCAGCC C	921

(2) INFORMATION FOR SEQ ID NO:85:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC	420
TCCCTGCCCC AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT	480
GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG	540
GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGCTCCCC TGAGCTCCTG CCCCAGCCAG	600
GCCCTGCAGC TGGCAGGCTG CTTGAGCAA CTCCATAGCG GCCTTTCT CTACCAAGGGG	660
CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGTC CCACCTTGGA CACACTGCAG	720
CTGGACGTG CCGACTTTGC CACCACCATC TGGCAGCAGA TGGAAGAACT GGGAAATGGCC	780
CCTGCCCTGC AGCCCACCCA GGGTGCCATG CCGGCCTTCG CCTCTGCTTT CCAGCGCCGG	840
GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT	900
CTACGCCACC TTGCGCAGCC C	921

(2) INFORMATION FOR SEQ ID NO:86:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 732 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

ATGGCTAAGT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGGCCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT	420
GAAATTATAC ATCACTTAAA GAGACCACCT GCACCTTTGC TGGACCCGAA CAACCTCAAT	480
GACGAAGACG TCTCTATCCT GATGGAACGA AACCTTCGAC TTCCAAACCT GGAGAGCTTC	540
GTAAGGGCTG TCAAGAACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC	600
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA	660
GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC TGGTTACCCCT TGAGCAAGCG	720
CAGGAACAAAC AG	732

(2) INFORMATION FOR SEQ ID NO:87:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 921 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

ATGGCTAAGT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGGCCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTA CACCATTGGG CCCTGCCAGC	420
TCCCTGCCCG AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGGAAGAT CCAGGGCGAT	480

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GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC CGAGGAGCTG	540
GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC TGAGCTCCTG CCCCAGCCAG	600
GCCCTGCAGC TGGCAGGCTG CTTGAGCAA CTCCATAGCG GCCTTTCTT CTACCAGGGG	660
CTCCTGCAGG CCCTGGAAGG GATATCCCC GAGTTGGTC CCACCTTGGA CACACTGCAG	720
CTGGACGTCG CCGACTTGC CACCACCATC TGGCAGCAGA TGGAAAGAACT GGGATGGCC	780
CCTGCCCTGC AGCCCACCCA GGGTGCATG CCGGCCTTCG CCTCTGCTT CCAGCGCCGG	840
GCAGGAGGGG TCCTGGTTGC TAGCCATCTG CAGAGCTTCC TGGAGGTGTC GTACCGCGTT	900
CTACGCCACC TTGGCAGCC C	921

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 732 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG GTGGTTCTGG CGCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT	420
GAAATTATAAC ATCACTTAAA GAGACCACCT GCACCTTTGC TGGACCCGAA CAACCTCAAT	480
GACGAAGACG TCTCTATCCT GATGGAACGA AACCTTCGAC TTCCAAACCT GGAGAGCTTC	540
GTAAGGGCTG TCAAGAACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC	600
CAACCATGTC TGCCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA	660
GGTGACTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC TGGTTACCCCT TGAGCAAGCG	720
CAGGAACAAAC AG	732

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 966 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA	60
CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGGA GCAAGCGCAG GAACAACAGT ACCTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC CGTCTCCTCC GTCTAAAGAA	420
TCTCTATAAT CTCCAAACAT GGCTACACCA TTGGGCCCTG CCAGCTCCCT GCCCCAGAGC	480
TTCCTGCTCA AGTCTTTAGA GCAAGTGAGG AAGATCCAGG GCGATGGCGC AGCGCTCCAG	540
GAGAAGCTGT GTGCCACCTA CAAGCTGTGC CACCCCGAGG AGCTGGTGCT GCTGGACAC	600
TCTCTGGGCA TCCCCTGGC TCCCCTGAGC TCCTGCCCA GCCAGGCCCT GCAGCTGGCA	660
GGCTGCTTGA GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG	720
GAAGGGATAT CCCCGAGTT GGGTCCCACC TTGGACACAC TGCAGCTGGA CGTCGCCGAC	780
TTTGCACCA CCATCTGGCA GCAGATGGAA GAACTGGAA TGGCCCTGCT CCTGCAGCCC	840
ACCCAGGGTG CCATGCCGGC CTTCGCCTCT GCTTCCAGC GCCGGGCAGG AGGGGCTCTG	900
GTTGCTAGCC ATCTGCAGAG CTTCCCTGGAG GTGTCGTACC GCGTTCTACG CCACCTTGCG	960
CAGCCC	966

(2) INFORMATION FOR SEQ ID NO:90:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 777 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTGCA

60

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CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT CTATCCTGAT GGAACGAAAC	120
CTTCGACTTC CAAACCTGGA GAGCTCGTA AGGGCTGTCA AGAACTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACC	300
TTCTATCTGG TTACCCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAAAC CGTCTCCTCC GTCTAAAGAA	420
TCTCATAAAT CTCCAAACAT GGCTAACTGC TCTATAATGA TCGATGAAAT TATACATCAC	480
TTAAAGAGAC CACCTGCACC TTTGCTGGAC CCGAACAAACC TCAATGACGA AGACGTCTCT	540
ATCCTGATGG AACGAAACCT TCGACTTCCA AACCTGGAGA GCTTCGTAAG GGCTGTCAAG	600
AACTTAGAAA ATGCATCAGG TATTGAGGCA ATTCTTCGTA ATCTCAAAC ATGTCTGCC	660
TCTGCCACGG CCGCACCCCTC TCGACATCCA ATCATCATCA AGGCAGGTGA CTGGCAAGAA	720
TTCCCGGAAA AACTGACGTT CTATCTGGTT ACCCTTGAGC AAGCGCAGGA ACAACAG	777

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 41 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

AATTCCGGGA AAAACTGACG TTCTATCTGG TTACCCCTTGA G

41

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 46 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

CTGCGCTTGC TCAAGGGTAA CCAGATAGAA CGTCAGTTT TCCCGG

46

(2) INFORMATION FOR SEQ ID NO:93:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

CAAGCGCAGG AACAAACAGTA CGTAATCGAG GGAAGGATT

39

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

ACCCGGGGAA ATCCTTCCCT CGATTACGTA CTGTTGTTC

39

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 63 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

TCCCCGGGTG GTGGTTCTGG CGGCGGCCTCC AACATGTAAG GTACCGCATG CAAGCTTAGA

60

TCT

63

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 58 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

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- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

AGCTAGATCT AAGCTTGCAT GCGGTACCTT ACATGTTGGA GCCGCCGCCA GAACCACC

58

- (2) INFORMATION FOR SEQ ID NO:97:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 74 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

CCGGGTGAAC CGTCTGGTCC AATCTCTACT ATCAACCCGT CTCCTCCGTC TAAAGAATCT

60

CATAAAATCTC CAAA

74

- (2) INFORMATION FOR SEQ ID NO:98:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 74 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

CATGTTGGA GATTTATGAG ATTCTTTAGA CGGAGGAGAC GGGTTGATAG TAGAGATTGG

60

ACCAGACGGT TCAC

74

- (2) INFORMATION FOR SEQ ID NO:99:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 68 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

CTAGCCATCT GCAGAGCTTC CTGGAGGTGT CGTACCGCGT TCTACGCCAC CTTGCGCAGC	60
CCTACGTA	68

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 68 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

AGCTTACGTA GGGCTGCGCA AGGTGGCGTA GAACGCGGTA CGACACCTCC AGGAAGCTCT	60
GCAGATGG	68

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

GTAATCGAGG GAAAGATTTC C	21
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(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

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CCGGGGAAAT CTTTCCCTCG ATTAC

25

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 21 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

GTAGAGGGCG GTGGAGGCTC C

21

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

CCGGGGAGCC TCCACCGCCC TCTAC

25

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 58 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

CATGGCACCA GCAAGATCAC CATCACCATC AACTAACCT TGGAACATG TGAATGCC

58

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 52 base pairs
- (B) TYPE: nucleic acid

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- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

CATTCACATG TTCCCAAGGT TGAGTTGATG GTGATGGTGA TCTTGCTGGT GC

52

- (2) INFORMATION FOR SEQ ID NO:107:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 66 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

CTGCCAGCTC CCTGCCAG AGCTTCCTGC TCAAAGTCTTT AGAGCAAGTG AGGAAGATCC

60

AGGGCG

66

- (2) INFORMATION FOR SEQ ID NO:108:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 66 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

CTGGATCTTC CTCACTTGCT CTAAAGACTT GAGCAGGAAG CTCTGGGCA GGGAGCTGGC

60

AGGGCC

66

- (2) INFORMATION FOR SEQ ID NO:109:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 48 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

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- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

AGCTTACCTG CCATGGCTCC AGTACCACCA GGTGAAGATT CCAAAGAT

48

(2) INFORMATION FOR SEQ ID NO:110:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 40 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

TTGGAATCTT CACCTGGTGG TACTGGAGCC ATGGCAGGTA

40

(2) INFORMATION FOR SEQ ID NO:111:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

AGCTTCCATG GCTACCCCCC TGGGCC

26

(2) INFORMATION FOR SEQ ID NO:112:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
(A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

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CAGGGGGGTA GCCATGGA

18

(2) INFORMATION FOR SEQ ID NO:113:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

CATGGCTACA CCATTGGGCC

20

(2) INFORMATION FOR SEQ ID NO:114:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

CAATGGTGTA GC

12

(2) INFORMATION FOR SEQ ID NO:115:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 20 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

CATGGCTACA CCATTAGGAC

20

(2) INFORMATION FOR SEQ ID NO:116:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 12 base pairs
- (B) TYPE: nucleic acid

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- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

TAATGGTGTA GC

12

- (2) INFORMATION FOR SEQ ID NO:117:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

CCTGTCAACC CGGGCGGCCGG CTCTGGTGGT

30

- (2) INFORMATION FOR SEQ ID NO:118:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

TCATAATACA TGTTACCGGA ACGGAGCCGC C

31

- (2) INFORMATION FOR SEQ ID NO:119:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

ATCGTCTGAC CTCCCGGGAC CTCCTGTCAA TGCT

34

(2) INFORMATION FOR SEQ ID NO:120:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

AGCGTTTGAC ATGTTTCAT AATCAAAATC

30

(2) INFORMATION FOR SEQ ID NO:121:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
115 120 125

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Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140

Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160

Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175

Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190

Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205

Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240

Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255

Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270

Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300

Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:122:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala

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50

55

60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140

Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160

Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175

Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190

Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205

Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240

Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255

Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270

Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300

Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:123:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Ser Gly Gly
115 120 125

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
130 135 140

Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
145 150 155 160

Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
165 170 175

Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
180 185 190

Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
195 200 205

Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
210 215 220

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
225 230 235 240

Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
245 250 255

Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
260 265 270

Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
275 280 285

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
290 295 300

Ala Gln Pro

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305

(2) INFORMATION FOR SEQ ID NO:124:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly
115 120 125

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
130 135 140

Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160

Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
165 170 175

Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
180 185 190

Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
195 200 205

Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
210 215 220

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
225 230 235 240

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Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
260 265 270

Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
275 280 285

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
290 295 300

Ala Gln Pro
305

(2) INFORMATION FOR SEQ ID NO:125:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 244 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 . 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly
115 120 125

Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
130 135 . 140

His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
145 . 150 155 160

Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asp Ile Arg Arg Thre Pro

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165 170 175

Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly
180 185 190

Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
195 200 205

Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
210 215 220

Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala
225 230 235 240

Gln Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:126:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 244 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser Gly Gly
115 120 125

Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
130 135 140

His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn
145 150 155 160

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Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
 165 170 175
 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly
 180 185 190
 Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
 195 200 205
 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
 210 215 220
 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala
 225 230 235 240
 Gln Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:127:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 244 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110
 Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser Gly Gly
 115 120 125
 Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
 130 135 140
 His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn

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145	150	155	160
Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn			
165		170	175
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly			
180		185	190
Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr			
195		200	205
Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln			
210		215	220
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala			
225		230	235
Gln Glu Gln Gln			

(2) INFORMATION FOR SEQ ID NO:128:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 322 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp			
20		25	30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala			
35		40	45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50		55	60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65		70	75
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85		90	95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100		105	110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro			
115		120	125
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser			
130		135	140

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Pro	Asn	Met	Ala	Thr	Pro	Leu	Gly	Pro	Ala	Ser	Ser	Leu	Pro	Gln	Ser
145					150				155				160		
Phe	Leu	Leu	Lys	Cys	Leu	Glu	Gln	Val	Arg	Lys	Ile	Gln	Gly	Asp	Gly
					165			170					175		
Ala	Ala	Leu	Gln	Glu	Lys	Leu	Cys	Ala	Thr	Tyr	Lys	Leu	Cys	His	Pro
					180			185				190			
Glu	Glu	Leu	Val	Leu	Leu	Gly	His	Ser	Leu	Gly	Ile	Pro	Trp	Ala	Pro
					195			200			205				
Leu	Ser	Ser	Cys	Pro	Ser	Gln	Ala	Leu	Gln	Leu	Ala	Gly	Cys	Leu	Ser
					210			215			220				
Gln	Leu	His	Ser	Gly	Leu	Phe	Leu	Tyr	Gln	Gly	Leu	Leu	Gln	Ala	Leu
					225			230			235			240	
Glu	Gly	Ile	Ser	Pro	Glu	Leu	Gly	Pro	Thr	Leu	Asp	Thr	Leu	Gln	Leu
					245			250			255				
Asp	Val	Ala	Asp	Phe	Ala	Thr	Thr	Ile	Trp	Gln	Gln	Met	Glu	Glu	Leu
					260			265			270				
Gly	Met	Ala	Pro	Ala	Leu	Gln	Pro	Thr	Gln	Gly	Ala	Met	Pro	Ala	Phe
					275			280			285				
Ala	Ser	Ala	Phe	Gln	Arg	Arg	Ala	Gly	Gly	Val	Leu	Val	Ala	Ser	His
					290			295			300				
Leu	Gln	Ser	Phe	Leu	Glu	Val	Ser	Tyr	Arg	Val	Leu	Arg	His	Leu	Ala
					305			310			315			320	
Gln	Pro														

(2) INFORMATION FOR SEQ ID NO:129:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 322 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1					5				10			15			
Arg	Pro	Pro	Asn	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ser	Glu	Asp
					20			25			30				
Met	Asp	Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Thr	Pro	Asn	Leu	Leu	Ala
					35			40			45				
Phe	Val	Arg	Ala	Val	Lys	His	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala

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50	55	60
Ile	Leu	Arg
Asn	Leu	Gln
Leu	Pro	Cys
65	70	75
Ser	Ala	Thr
Ala	Ala	Pro
Ser	Arg	His
Arg	His	Pro
Ile	Ile	Ile
Lys	Ala	Gly
85	90	95
Glu	Lys	Leu
Lys	Leu	Thr
Phe	Tyr	Leu
100	105	110
Gln	Tyr	Val
Tyr	Val	Ile
Glu	Gly	Lys
115	120	125
Ile	Ser	Thr
Ser	Ile	Asn
Asn	Pro	Ser
Pro	Pro	Pro
130	135	140
Ser	Lys	Glu
His	Ser	Ser
Lys	Ser	His
Gln	Gln	Gln
145	150	155
160		
Phe	Leu	Leu
Lys	Cys	Leu
Leu	Glu	Gln
165	170	175
Gln	Gly	Asp
Ala	Ala	Leu
Gln	Glu	Lys
Leu	Cys	Ala
180	185	190
Thr	Tyr	Lys
Lys	Leu	Cys
His	Pro	
Glu	Glu	Leu
Leu	Val	Leu
Leu	Gly	His
195	200	205
Ser	Ser	Ile
Cys	Pro	Pro
210	215	220
Gln	Ala	Leu
Leu	Gln	Gly
225	230	235
Ala	Leu	Cys
240		
Glu	Gly	Ile
Ile	Ser	Pro
Pro	Glu	Leu
Gly	Pro	Thr
245	250	255
Thr	Leu	Asp
Leu	Gln	Thr
Asp	Val	Leu
Val	Ala	Gly
Ala	Asp	Cys
Phe	Ala	Leu
260	265	270
Thr	Thr	Ile
Ile	Trp	Gln
Trp	Gln	Gln
Gln	Met	Ala
Met	Glu	Glu
Glu	Glu	Leu
275	280	285
Gly	Met	Ala
Met	Pro	Ala
Ala	Leu	Gln
Gln	Pro	Thr
290	295	300
Gly	Gly	Gly
Arg	Arg	Val
Ala	Gly	Leu
295	300	
Leu	Val	Val
305	310	315
Ala	Ala	Ala
Ser	Ser	Ser
Phe	Phe	Arg
Leu	Leu	Arg
Glu	Glu	Val
310	315	320
Val	Tyr	Arg
Ser	Arg	Val
Tyr	Val	Leu
Arg	Leu	Arg
315	320	
His	His	
Leu	Leu	
Ala	Ala	
Gln	Pro	

(2) INFORMATION FOR SEQ ID NO:130:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 322 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140

Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
 145 150 155 160

Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
 165 170 175

Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
 180 185 190

Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
 195 200 205

Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
 210 215 220

Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
 225 230 235 240

Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
 245 250 255

Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
 260 265 270

Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
 275 280 285

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Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His
 290 295 300

Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
 305 310 315 320

Gln Pro

(2) INFORMATION FOR SEQ ID NO:131:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 .85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140

Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 145 150 155 160

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
 165 170 175

Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
 180 185 190

Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile

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195

200

205

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 210 215 220

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 225 230 235 240

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 245 250 255

Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:132:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140

Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 145 150 155 160

Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
 165 170 175

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Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu
 180 185 190

Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile
 195 200 205

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 210 215 220

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 225 230 235 240

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 245 250 255

Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:133:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 259 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140

Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His

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145	150	155	160
Leu Lys Arg Pro Prc Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser			
165		170	175
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu			
180	185		190
Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile			
195	200		205
Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala			
210	215		220
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu			
225	230	235	240
Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln			
245		250	255
Glu Gln Gln			

(2) INFORMATION FOR SEQ ID NO:134:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1				5					10					15	
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp															
				20				25				30			
Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser															
				35				40				45			
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala															
				50				55				60			
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro															
				65.				70				75			80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg															
				85				90				95			
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln															
				100				105				110			
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly															
				115				120				125			

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Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140

Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
 145 150 155 160

Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
 165 170 175

Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
 180 185 190

Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
 195 200 205

Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala
 210 215 220

Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln
 225 230 235 240

Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
 245 250 255

Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
 260 265 270

Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
 275 280 285

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu
 290 295 300

Ala Gln Pro
 305

(2) INFORMATION FOR SEQ ID NO:135:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30

Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala

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50	55	60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro		
65	70	75
Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg		
85	90	95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln		
100	105	110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly		
115	120	125
Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln		
130	135	140
Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp		
145	150	155
Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His		
165	170	175
Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala		
180	185	190
Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu		
195	200	205
Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala		
210	215	220
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln		
225	230	235
240		
Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu		
245	250	255
Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala		
260	265	270
Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser		
275	280	285
His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu		
290	295	300
Ala Gln Pro		
305		

(2) INFORMATION FOR SEQ ID NO:136:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 244 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30

Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His
 130 135 140

His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
 145 150 155 160

Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn
 165 170 175

Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly
 180 185 190

Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
 195 200 205

Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln
 210 215 220

Glu Phe Arg Glu Lys Leu Thr Phe Tyr. Leu Val Thr Leu Glu Gln Ala
 225 230 235 240

Gln Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:137:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1						5				10					15
Arg	Pro	Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Asp	Glu	Asp
						20				25					30
Val	Ser	Ile	Leu	Met	Asp	Arg	Asn	Leu	Arg	Leu	Pro	Asn	Leu	Glu	Ser
						35				40					45
Phe	Val	Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala
						50				55					60
Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro
						65				70			75		80
Ser	Arg	His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg
						85				90					95
Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln	Glu	Gln
						100				105					110
Gln	Tyr	Val	Ile	Glu	Gly	Arg	Ile	Ser	Pro	Gly	Glu	Pro	Ser	Gly	Pro
						115				120					125
Ile	Ser	Thr	Ile	Asn	Pro	Ser	Pro	Pro	Ser	Lys	Glu	Ser	His	Lys	Ser
						130				135					140
Pro	Asn	Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His
						145				150			155		160
Leu	Lys	Arg	Pro	Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Asp
						165				170					175
Glu	Asp	Val	Ser	Ile	Leu	Met	Asp	Arg	Asn	Leu	Arg	Leu	Pro	Asn	Leu
						180				185					190
Glu	Ser	Phe	Val	Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser	Gly	Ile
						195				200					205
Glu	Ala	Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala
						210				215					220
Ala	Pro	Ser	Arg	His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu
						225				230			235		240
Phe	Arg	Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln
						245				250					255
Glu	Gln	Gln													

(2) INFORMATION FOR SEQ ID NO:138:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
20 25 30

Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro
115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser
130 135 140

Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
145 150 155 160

Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
165 170 175

Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
180 185 190

Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro
195 200 205

Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser
210 215 220

Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu
225 230 235 240

Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
245 250 255

Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
260 265 270

Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe

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275	280	285
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Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His		
290	295	300

Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala			
305	310	315	320

Gln Pro

(2) INFORMATION FOR SEQ ID NO:139:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 349 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp		
20	25	30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala		
35	40	45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala		
50	55	60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg		
85	90	95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln		
100	105	110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala		
115	120	125

Gly Gly Gly Ser Gly Gly Ser Gly Gly Ser Glu Gly Gly Gly		
130	135	140

Ser Glu Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser			
145	150	155	160

Gly Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala Thr		
165	170	175

Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser		
180	185	190

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Leu	Glu	Gln	Val	Arg	Lys	Ile	Gln	Gly	Asp	Gly	Ala	Ala	Leu	Gln	Glu
195							200							205	
Lys	Leu	Cys	Ala	Thr	Tyr	Lys	Leu	Cys	His	Pro	Glu	Glu	Leu	Val	Leu
210							215							220	
Leu	Gly	His	Ser	Leu	Gly	Ile	Pro	Trp	Ala	Pro	Leu	Ser	Ser	Cys	Pro
225							230					235		240	
Ser	Gln	Ala	Leu	Gln	Leu	Ala	Gly	Cys	Leu	Ser	Gln	Leu	His	Ser	Gly
245												250		255	
Leu	Phe	Leu	Tyr	Gln	Gly	Leu	Leu	Gln	Ala	Leu	Glu	Gly	Ile	Ser	Pro
260											265		270		
Glu	Leu	Gly	Pro	Thr	Leu	Asp	Thr	Leu	Gln	Leu	Asp	Val	Ala	Asp	Phe
275												280		285	
Ala	Thr	Thr	Ile	Trp	Gln	Gln	Met	Glu	Glu	Leu	Gly	Met	Ala	Pro	Ala
290							295					300			
Leu	Gln	Pro	Thr	Gln	Gly	Ala	Met	Pro	Ala	Phe	Ala	Ser	Ala	Phe	Gln
305							310					315		320	
Arg	Arg	Ala	Gly	Gly	Val	Leu	Val	Ala	Ser	His	Leu	Gln	Ser	Phe	Leu
325												330		335	
Glu	Val	Ser	Tyr	Arg	Val	Leu	Arg	His	Leu	Ala	Gln	Pro			
340												345			

(2) INFORMATION FOR SEQ ID NO:140:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 64 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

GGATCCACCA	TGAGCCGCCT	GCCCCGTCTG	CTCCTGCTCC	AACTCCTGGT	CCGCCCGGCC	60
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ATGG	64
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(2) INFORMATION FOR SEQ ID NO:141:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 259 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1					5					10				15	
Arg	Pro	Pro	Asn	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ser	Glu	Asp
					20				25				30		
Met	Asp	Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Thr	Pro	Asn	Leu	Leu	Ala
				35				40				45			
Phe	Val	Arg	Ala	Val	Lys	His	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala
				50			55				60				
Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro
	65				70				75			80			
Ser	Arg	His	Pro	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg	
				85				90				95			
Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln	Glu	Gln
				100			105				110				
Gln	Tyr	Val	Ile	Glu	Gly	Arg	Ile	Ser	Pro	Gly	Gly	Ser	Gly	Gly	
				115			120				125				
Gly	Ser	Asn	Met	Ala	Pro	Ala	Arg	Ser	Pro	Ser	Pro	Ser	Thr	Gln	Pro
				130			135				140				
Trp	Glu	His	Val	Asn	Ala	Ile	Gln	Glu	Ala	Arg	Arg	Leu	Leu	Asn	Leu
				145			150				155			160	
Ser	Arg	Asp	Thr	Ala	Ala	Glu	Met	Asn	Glu	Thr	Val	Glu	Val	Ile	Ser
				165				170				175			
Glu	Met	Phe	Asp	Leu	Gln	Glu	Pro	Thr	Cys	Leu	Gln	Thr	Arg	Leu	Glu
				180				185				190			
Leu	Tyr	Lys	Gln	Gly	Leu	Arg	Gly	Ser	Leu	Thr	Lys	Leu	Lys	Gly	Pro
				195				200				205			
Leu	Thr	Met	Met	Ala	Ser	His	Tyr	Lys	Gln	His	Cys	Pro	Pro	Thr	Pro
				210			215				220				
Glu	Thr	Ser	Cys	Ala	Thr	Gln	Ile	Ile	Thr	Phe	Glu	Ser	Phe	Lys	Glu
				225			230				235			240	
Asn	Leu	Lys	Asp	Phe	Leu	Leu	Val	Ile	Pro	Phe	Asp	Cys	Trp	Glu	Pro
				245				250				255			
Val	Gln	Glu													

(2) INFORMATION FOR SEQ ID NO:142:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 301 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
100 105 110

Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala
115 120 125

Gly Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Glu Gly Gly Gly
130 135 140

Ser Glu Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Gly Ser
145 150 155 160

Gly Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn Met Ala Pro
165 170 175

Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp Glu His Val Asn Ala
180 185 190

Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser Arg Asp Thr Ala Ala
195 200 205

Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu Met Phe Asp Leu Gln
210 215 220

Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu Tyr Lys Gln Gly Leu
225 230 235 240

Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu Thr Met Met Ala Ser
245 250 255

His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu Thr Ser Cys Ala Thr
260 265 270

Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp Phe Leu
275 280 285

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Leu	Val	Ile	Pro	Phe	Asp	Cys	Trp	Glu	Pro	Val	Gln	Glu
290						295					300	

(2) INFORMATION FOR SEQ ID NO:143:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 335 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1					5				10				15		

Arg	Pro	Pro	Asn	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ser	Glu	Asp
					20				25				30		

Met	Asp	Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Thr	Pro	Asn	Leu	Leu	Ala
					35			40				45			

Phe	Val	Arg	Ala	Val	Lys	His	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala
					50			55				60			

Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro
					65			70				75			80

Ser	Arg	His	Pro	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg	
					85			90				95			

Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln	Glu	Gln
					100			105				110			

Gln	Tyr	Val	Pro	Val	Asn	Ala	Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Ser
					115			120				125			

Gly	Gly	Ser	Glu	Gly	Gly	Ser	Glu	Gly	Gly	Ser	Glu	Gly	Gly	Ser	
					130			135				140			

Gly	Ser	Glu	Gly	Gly	Ser	Gly	Gly	Ser	Gly	Ser	Gly	Asn	Met		
					145			150				155			160

Ala	Thr	Pro	Leu	Gly	Pro	Ala	Ser	Ser	Leu	Pro	Gln	Ser	Phe	Leu	Leu
					165			170				175			

Lys	Cys	Leu	Glu	Gln	Val	Arg	Lys	Ile	Gln	Gly	Asp	Gly	Ala	Ala	Leu
					180			185				190			

Gln	Glu	Lys	Leu	Cys	Ala	Thr	Tyr	Lys	Leu	Cys	His	Pro	Glu	Glu	Leu
					195			200				205			

Val	Leu	Leu	Gly	His	Ser	Leu	Gly	Ile	Pro	Trp	Ala	Pro	Leu	Ser	Ser
					210			215				220			

Cys	Pro	Ser	Gln	Ala	Leu	Gln	Leu	Ala	Gly	Cys	Leu	Ser	Gln	Leu	His
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

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225	230	235	240
Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile			
245	250		255
Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala			
260	265		270
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala			
275	280		285
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala			
290	295		300
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser			
305	310		315
Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro			
325	330		335

(2) INFORMATION FOR SEQ ID NO:144:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 274 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15
Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp			
20	25		30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala			
35	40		45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50	55		60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70		75
			80
Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85	90		95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100	105		110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro			
115	120		125
Ile Ser Thr Ile Asn Pro Ser Pro Ser Lys Glu Ser His Lys Ser			
130	135		140

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Pro Asn Met Ala Pro Ala Arg Ser Pro Ser Pro Ser Thr Gln Pro Trp
 145 150 155 160
 Glu His Val Asn Ala Ile Gln Glu Ala Arg Arg Leu Leu Asn Leu Ser
 165 170 175
 Arg Asp Thr Ala Ala Glu Met Asn Glu Thr Val Glu Val Ile Ser Glu
 180 185 190
 Met Phe Asp Leu Gln Glu Pro Thr Cys Leu Gln Thr Arg Leu Glu Leu
 195 200 205
 Tyr Lys Gln Gly Leu Arg Gly Ser Leu Thr Lys Leu Lys Gly Pro Leu
 210 215 220
 Thr Met Met Ala Ser His Tyr Lys Gln His Cys Pro Pro Thr Pro Glu
 225 230 235 240
 Thr Ser Cys Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn
 245 250 255
 Leu Lys Asp Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val
 260 265 270
 Gln Glu

(2) INFORMATION FOR SEQ ID NO:145:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 317 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15
 Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30
 Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45
 Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60
 Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80
 Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95
 Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln

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100	105	110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly		
115	120	125
Gly Ser Asn Met Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val		
130	135	140
Ala Ala Pro His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys		
145	150	155
Gln Ile Arg Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr		
165	170	175
Cys Asn Lys Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu		
180	185	190
Asn Asn Leu Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln		
195	200	205
Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu		
210	215	220
Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser		
225	230	235
Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile		
245	250	255
Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro		
260	265	270
Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn		
275	280	285
Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys		
290	295	300
Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg Gln Met		
305	310	315

(2) INFORMATION FOR SEQ ID NO:146:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu		
1	5	10
Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala		
20	25	30

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Leu	Gln	Glu	Lys	Leu	Cys	Ala	Thr	Tyr	Lys	Leu	Cys	His	Pro	Glu	Glu
35															45
Leu	Val	Leu	Leu	Gly	His	Ser	Leu	Gly	Ile	Pro	Trp	Ala	Pro	Leu	Ser
50															60
Ser	Cys	Pro	Ser	Gln	Ala	Leu	Gln	Leu	Ala	Gly	Cys	Leu	Ser	Gln	Leu
65															80
His	Ser	Gly	Leu	Phe	Leu	Tyr	Gln	Gly	Leu	Leu	Gln	Ala	Leu	Glu	Gly
															95
Ile	Ser	Pro	Glu	Leu	Gly	Pro	Thr	Leu	Asp	Thr	Leu	Gln	Leu	Asp	Val
															100 105 110
Ala	Asp	Phe	Ala	Thr	Thr	Ile	Trp	Gln	Gln	Met	Glu	Glu	Leu	Gly	Met
															115 120 125
Ala	Pro	Ala	Leu	Gln	Pro	Thr	Gln	Gly	Ala	Met	Pro	Ala	Phe	Ala	Ser
															130 135 140
Ala	Phe	Gln	Arg	Arg	Ala	Gly	Gly	Val	Leu	Val	Ala	Ser	His	Leu	Gln
															145 150 155 160
Ser	Phe	Leu	Glu	Val	Ser	Tyr	Arg	Val	Leu	Arg	His	Leu	Ala	Gln	Pro
															165 170 175
Tyr	Val	Ile	Glu	Gly	Arg	Ile	Ser	Pro	Gly	Gly	Ser	Gly	Gly	Gly	
															180 185 190
Ser	Asn	Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His
															195 200 205
Leu	Lys	Arg	Pro	Pro	Asn	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ser
															210 215 220
Glu	Asp	Met	Asp	Ile	Leu	Met	Glu	Arg	Asn	Leu	Arg	Thr	Pro	Asn	Leu
															225 230 235 240
Leu	Ala	Phe	Val	Arg	Ala	Val	Lys	His	Leu	Glu	Asn	Ala	Ser	Gly	Ile
															245 250 255
Glu	Ala	Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala
															260 265 270
Ala	Pro	Ser	Arg	His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu
															275 280 285
Phe	Arg	Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln
															290 295 300
Glu	Gln	Gln													
															305

(2) INFORMATION FOR SEQ ID NO:147:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
100 105 110

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly Gly
180 185 190

Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
195 200 205

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
210 215 220

Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
225 230 235 240

Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
245 250 255

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
260 265 270

Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu
275 280 285

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Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 290 295 300

Glu Gln Gln
 305

(2) INFORMATION FOR SEQ ID NO:148:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 337 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
 65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Pro Gln Pro Pro Val Asn Ala Gly Gly Ser Gly Gly Gly
 180 185 190

Ser Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser Glu
 195 200 205

Gly Gly Gly Ser Glu Gly Gly Ser Gly Gly Ser Gly

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210

215

220

Asp Phe Asp Tyr Glu Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu
 225 230 235 240

Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn
 245 250 255

Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg
 260 265 270

Leu Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 275 280 285

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 290 295 300

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 305 310 315 320

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 325 330 335

Gln

(2) INFORMATION FOR SEQ ID NO:149:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
 35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
 65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110

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Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile
 180 185 190

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
 195 200 205

Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
 210 215 220

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu
 225 230 235 240

Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu
 245 250 255

Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
 260 265 270

Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
 275 280 285

Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe
 290 295 300

Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu
 305 310 315 320

Gln Gln

(2) INFORMATION FOR SEQ ID NO:150:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala

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20	25	30
Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu		
35	40	45
Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser		
50	55	60
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu		
65	70	75
80		
His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly		
85	90	95
Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val		
100	105	110
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met		
115	120	125
Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser		
130	135	140
Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln		
145	150	155
160		
Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro		
165	170	175
Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile		
180	185	190
Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro		
195	200	205
Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu		
210	215	220
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu		
225	230	235
240		
Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu		
245	250	255
Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu		
260	265	270
Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala		
275	280	285
Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe		
290	295	300
Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu		
305	310	315
320		
Gln Gln		

(2) INFORMATION FOR SEQ ID NO:151:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 349 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:151:

Met	Ala	Thr	Pro	Leu	Gly	Pro	Ala	Ser	Ser	Leu	Pro	Gln	Ser	Phe	Leu
1				5						10					15
Leu	Lys	Cys	Leu	Glu	Gln	Val	Arg	Lys	Ile	Gln	Gly	Asp	Gly	Ala	Ala
				20				25						30	
Leu	Gln	Glu	Lys	Leu	Cys	Ala	Thr	Tyr	Lys	Leu	Cys	His	Pro	Glu	Glu
	35						40					45			
Leu	Val	Leu	Leu	Gly	His	Ser	Leu	Gly	Ile	Pro	Trp	Ala	Pro	Leu	Ser
	50				55				60						
Ser	Cys	Pro	Ser	Gln	Ala	Leu	Gln	Leu	Ala	Gly	Cys	Leu	Ser	Gln	Leu
	65					70				75				80	
His	Ser	Gly	Leu	Phe	Leu	Tyr	Gln	Gly	Leu	Leu	Gln	Ala	Leu	Glu	Gly
		85					90					95			
Ile	Ser	Pro	Glu	Leu	Gly	Pro	Thr	Leu	Asp	Thr	Leu	Gln	Leu	Asp	Val
		100					105					110			
Ala	Asp	Phe	Ala	Thr	Thr	Ile	Trp	Gln	Gln	Met	Glu	Glu	Leu	Gly	Met
		115						120				125			
Ala	Pro	Ala	Leu	Gln	Pro	Thr	Gln	Gly	Ala	Met	Pro	Ala	Phe	Ala	Ser
		130				135				140					
Ala	Phe	Gln	Arg	Arg	Ala	Gly	Gly	Val	Leu	Val	Ala	Ser	His	Leu	Gln
		145				150				155			160		
Ser	Phe	Leu	Glu	Val	Ser	Tyr	Arg	Val	Leu	Arg	His	Leu	Ala	Gln	Pro
		165					170				175				
Tyr	Val	Ile	Glu	Gly	Arg	Ile	Ser	Pro	Gln	Pro	Pro	Val	Asn	Ala	Gly
			180				185				190				
Gly	Gly	Ser	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Glu	Gly	Gly	Gly	Ser	
		195				200				205					
Glu	Gly	Gly	Gly	Ser	Glu	Gly	Gly	Ser	Glu	Gly	Gly	Gly	Ser	Gly	
		210				215				220					
Gly	Gly	Ser	Gly	Ser	Gly	Asp	Phe	Asp	Tyr	Glu	Asn	Met	Ala	Asn	Cys
		225				230				235			240		
Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys	Arg	Pro	Pro	Asn
			245				250				255				

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Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu
 260 265 270

Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala
 275 280 285

Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn
 290 295 300

Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro
 305 310 315 320

Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr
 325 330 335

Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 340 345

(2) INFORMATION FOR SEQ ID NO:152:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30

Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 130 135 140

Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp

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145	150	155	160
Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His			
165		170	175
Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala			
180		185	190
Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu			
195	200	205	
Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala			
210	215	220	
Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln			
225	230	235	240
Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu			
245		250	255
Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala			
260		265	270
Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser			
275	280	285	
His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu			
290	295	300	
Ala Gln Pro			
305			

(2) INFORMATION FOR SEQ ID NO:153:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 244 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys			
1	5	10	15
Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp			
20		25	30
Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser			
35	40	45	
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala			
50	55	60	
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro			
65	70	75	80

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Ser	Arg	His	Pro	Ile	Ile	Lys	Ala	Gly	Asp	Trp	Gln	Glu	Phe	Arg
				85				90				95		
Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln	Ala	Gln	Glu
				100			105				110			
Gln	Tyr	Val	Glu	Gly	Gly	Gly	Ser	Pro	Gly	Gly	Ser	Gly	Gly	
		115			120					125				
Gly	Ser	Asn	Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile
		130			135			140						
His	Leu	Lys	Arg	Pro	Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu
		145			150			155				160		
Asp	Glu	Asp	Val	Ser	Ile	Leu	Met	Asp	Arg	Asn	Leu	Arg	Leu	Pro
				165			170			175				
Leu	Glu	Ser	Phe	Val	Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser
				180			185			190				
Ile	Glu	Ala	Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala
				195			200			205				
Ala	Ala	Pro	Ser	Arg	His	Pro	Ile	Ile	Ile	Lys	Ala	Gly	Asp	Trp
				210			215			220				
Glu	Phe	Arg	Glu	Lys	Leu	Thr	Phe	Tyr	Leu	Val	Thr	Leu	Glu	Gln
		225			230			235			240			
Gln	Glu	Gln	Gln											

(2) INFORMATION FOR SEQ ID NO:154:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 322 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1					5				10			15			
Arg	Pro	Pro	Ala	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Asp	Glu	Asp
					20			25			30				
Val	Ser	Ile	Leu	Met	Asp	Arg	Asn	Leu	Arg	Leu	Pro	Asn	Leu	Glu	Ser
				35			40			45					
Phe	Val	Arg	Ala	Val	Lys	Asn	Leu	Glu	Asn	Ala	Ser	Gly	Ile	Glu	Ala
				50			55			60					
Ile	Leu	Arg	Asn	Leu	Gln	Pro	Cys	Leu	Pro	Ser	Ala	Thr	Ala	Ala	Pro

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65	70	75	80
Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg			
85		90	95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln			
100		105	110
Gln Tyr Val Ile Glu Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro			
115		120	125
Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser			
130		135	140
Pro Asn Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser			
145		150	155
Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly			
165		170	175
Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro			
180		185	190
Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro			
195		200	205
Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser			
210		215	220
Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu			
225		230	235
Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu			
245		250	255
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu			
260		265	270
Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe			
275		280	285
Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His			
290		295	300
Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala			
305		310	315
Gln Pro			

(2) INFORMATION FOR SEQ ID NO:155:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 259 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:155:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
 20 25 30

Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
 35 40 45

Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro
 115 120 125

Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser
 130 135 140

Pro Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 145 150 155 160

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 165 170 175

Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 180 185 190

Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 195 200 205

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 210 215 220

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 225 230 235 240

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 245 250 255

Glu Gln Gln

(2) INFORMATION FOR SEQ ID NO:156:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 322 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:156:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
1 5 10 15

Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu
65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
100 105 110

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

Tyr Val Glu Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
180 185 190

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
195 200 205

Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
210 215 220

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu
225 230 235 240

Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu
245 250 255

Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
260 265 270

Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala
275 280 285

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Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe
290 295 300

Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu
305 310 315 320

Gln Gln

(2) INFORMATION FOR SEQ ID NO:157:

- (i) SEQUENCE CHARACTERISTICS:

 - (A) LENGTH: 322 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:157:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
1 5 10 15

Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu
35 40 45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu
 65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
85 90 95

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
180 185 186

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro

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195	200	205
Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu		
210	215	220
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu		
225	230	235
Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu		
245	250	255
Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu		
260	265	270
Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala		
275	280	285
Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe		
290	295	300
Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu		
305	310	315
Gln Gln		

(2) INFORMATION FOR SEQ ID NO:158:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 307 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:

Met	Ala	Thr	Pro	Leu	Gly	Pro	Ala	Ser	Ser	Leu	Pro	Gln	Ser	Phe	Leu
1				5				10			15				
Leu Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala															
				20			25			30					
Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu															
				35			40			45					
Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser															
				50			55			60					
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu															
				65			70			75			80		
His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly															
				85			90			95					
Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val															
				100			105			110					

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Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser Gly Gly Ser Gly Gly
 180 185 190

Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 195 200 205

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 210 215 220

Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 225 230 235 240

Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 245 250 255

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 260 265 270

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu
 275 280 285

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 290 295 300

Glu Gln Gln
 305

(2) INFORMATION FOR SEQ ID NO:159:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 307 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
 1 5 10 15

Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala
 20 25 30

Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu

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35

40

45

Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser
 50 55 60

Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gly Leu
 65 70 75 80

His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
 85 90 95

Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 100 105 110

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met
 115 120 125

Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
 130 135 140

Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser Gly Gly Gly
 180 185 190

Ser Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
 195 200 205

Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
 210 215 220

Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu
 225 230 235 240

Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
 245 250 255

Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
 260 265 270

Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu
 275 280 285

Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln
 290 295 300

Glu Gln Gln
 305

(2) INFORMATION FOR SEQ ID NO:160:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 128 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:

Met	Ala	Pro	Ala	Arg	Ser	Pro	Ser	Pro	Ser	Thr	Gln	Pro	Trp	Glu	His
1				5				10					15		
Val	Asn	Ala	Ile	Gln	Glu	Ala	Arg	Arg	Leu	Leu	Asn	Leu	Ser	Arg	Asp
			20					25				30			
Thr	Ala	Ala	Glu	Met	Asn	Glu	Thr	Val	Glu	Val	Ile	Ser	Glu	Met	Phe
			35			40					45				
Asp	Leu	Gln	Glu	Pro	Thr	Cys	Leu	Gln	Thr	Arg	Leu	Glu	Leu	Tyr	Lys
			50			55			60						
Gln	Gly	Leu	Arg	Gly	Ser	Leu	Thr	Lys	Leu	Lys	Gly	Pro	Leu	Thr	Met
			65			70		75			80				
Met	Ala	Ser	His	Tyr	Lys	Gln	His	Cys	Pro	Pro	Thr	Pro	Glu	Thr	Ser
				85				90			95				
Cys	Ala	Thr	Gln	Ile	Ile	Thr	Phe	Glu	Ser	Phe	Lys	Glu	Asn	Leu	Lys
				100			105				110				
Asp	Phe	Leu	Leu	Val	Ile	Pro	Phe	Asp	Cys	Trp	Glu	Pro	Val	Gln	Glu
				115			120				125				

(2) INFORMATION FOR SEQ ID NO:161:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 176 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:

Met	Ala	Thr	Pro	Leu	Gly	Pro	Ala	Ser	Ser	Leu	Pro	Gln	Ser	Phe	Leu
1					5				10			15			
Leu	Lys	Cys	Leu	Glu	Gln	Val	Arg	Lys	Ile	Gln	Gly	Asp	Gly	Ala	Ala
			20				25				30				
Leu	Gln	Glu	Lys	Leu	Cys	Ala	Thr	Tyr	Lys	Leu	Cys	His	Pro	Glu	Glu
			35			40			45						
Leu	Val	Leu	Leu	Gly	His	Ser	Leu	Gly	Ile	Pro	Trp	Ala	Pro	Leu	Ser
			50			55			60						
Ser	Cys	Pro	Ser	Gln	Ala	Leu	Gln	Leu	Ala	Gly	Cys	Leu	Ser	Gln	Leu
			65			70			75			80			

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His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly			
85	90	95	
Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val			
100	105	110	
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met			
115	120	125	
Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser			
130	135	140	
Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln			
145	150	155	160
Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro			
165	170	175	

(2) INFORMATION FOR SEQ ID NO:162:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 176 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:162:

Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu			
1	5	10	15
Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala			
20	25	30	
Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu			
35	40	45	
Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser			
50	55	60	
Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu			
65	70	75	80
His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly			
85	90	95	
Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val			
100	105	110	
Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met			
115	120	125	
Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser			
130	135	140	

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Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln
 145 150 155 160

Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
 165 170 175

(2) INFORMATION FOR SEQ ID NO:163:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 186 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:163:

Met Ala Pro Val Pro Pro Gly Glu Asp Ser Lys Asp Val Ala Ala Pro
 1 5 10 15

His Arg Gln Pro Leu Thr Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg
 20 25 30

Tyr Ile Leu Asp Gly Ile Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys
 35 40 45

Ser Asn Met Cys Glu Ser Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu
 50 55 60

Asn Leu Pro Lys Met Ala Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe
 65 70 75 80

Asn Glu Glu Thr Cys Leu Val Lys Ile Ile Thr Gly Leu Leu Glu Phe
 85 90 95

Glu Val Tyr Leu Glu Tyr Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu
 100 105 110

Gln Ala Arg Ala Val Gln Met Ser Thr Lys Val Leu Ile Gln Phe Leu
 115 120 125

Gln Lys Lys Ala Lys Asn Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr
 130 135 140

Thr Asn Ala Ser Leu Leu Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu
 145 150 155 160

Gln Asp Met Thr Thr His Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu
 165 170 175

Gln Ser Ser Leu Arg Ala Leu Arg Gln Met
 180 185

(2) INFORMATION FOR SEQ ID NO:164:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 155 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

Met	Ala	Ser	Pro	Ala	Pro	Pro	Ala	Cys	Asp	Leu	Arg	Val	Leu	Ser	Lys
1															15

Leu	Leu	Arg	Asp	Ser	His	Val	Leu	His	Ser	Arg	Leu	Ser	Gln	Cys	Pro
															30
20		25													

Glu	Val	His	Pro	Leu	Pro	Thr	Pro	Val	Leu	Leu	Pro	Ala	Val	Asp	Phe
															45
35		40													

Ser	Leu	Gly	Glu	Trp	Lys	Thr	Gln	Met	Glu	Glu	Thr	Lys	Ala	Gln	Asp
															60
50		55													

Ile	Leu	Gly	Ala	Val	Thr	Leu	Leu	Glu	Gly	Val	Met	Ala	Ala	Arg	
65															80

Gln	Gln	Leu	Gly	Pro	Thr	Cys	Leu	Ser	Ser	Leu	Leu	Gly	Gln	Leu	Ser
															95
85		90													

Gly	Gln	Val	Arg	Leu	Leu	Gly	Ala	Leu	Gln	Ser	Leu	Leu	Gly	Thr	
															110
100		105													

Gln	Leu	Pro	Pro	Gln	Gly	Arg	Thr	Thr	Ala	His	Lys	Asp	Pro	Asn	Ala
															125
115		120													

Ile	Phe	Leu	Ser	Phe	Gln	His	Leu	Leu	Arg	Gly	Lys	Val	Arg	Phe	Leu
															140
130		135													

Met	Leu	Val	Gly	Gly	Ser	Thr	Leu	Cys	Val	Arg
145		150								

155

(2) INFORMATION FOR SEQ ID NO:165:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 286 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

Met	Ala	Asn	Cys	Ser	Ile	Met	Ile	Asp	Glu	Ile	Ile	His	His	Leu	Lys
1															15

Arg	Pro	Pro	Asn	Pro	Leu	Leu	Asp	Pro	Asn	Asn	Leu	Asn	Ser	Glu	Asp
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

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20	25	30
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala		
35	40	45
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala		
50	55	60
Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro		
65	70	75
Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg		
85	90	95
Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln		
100	105	110
Gln Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly		
115	120	125
Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val		
130	135	140
Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser		
145	150	155
160		
Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala		
165	170	175
Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys		
180	185	190
Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met		
195	200	205
Ala Ala Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly		
210	215	220
Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu		
225	230	235
240		
Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp		
245	250	255
Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val		
260	265	270
Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg		
275	280	285

(2) INFORMATION FOR SEQ ID NO:166:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 286 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: protein

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys
 1 5 10 15

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
 20 25 30

Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
 35 40 45

Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala
 50 55 60

Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro
 65 70 75 80

Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg
 85 90 95

Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln
 100 105 110

Gln Tyr Val Glu Gly Gly Ser Pro Gly Gly Ser Gly Gly
 115 120 125

Gly Ser Asn Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val
 130 135 140

Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser
 145 150 155 160

Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala
 165 170 175

Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys
 180 185 190

Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
 195 200 205

Ala Ala Arg Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
 210 215 220

Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu
 225 230 235 240

Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp
 245 250 255

Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val
 260 265 270

Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg
 275 280 285

(2) INFORMATION FOR SEQ ID NO:167:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 286 amino acids

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- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:

Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys
1 5 10 15

Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
20 25 30

Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe
35 40 45

Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp
50 55 60

Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg
65 70 75 80

Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser
85 90 95

Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
100 105 110

Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala
115 120 125

Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu
130 135 140

Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Tyr Val Ile Glu Gly
145 150 155 160

Arg Ile Ser Pro Gly Gly Ser Gly Gly Ser Asn Met Ala Asn
165 170 175

Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro
180 185 190

Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile
195 200 205

Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg
210 215 220

Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg
225 230 235 240

Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His
245 250 255

Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu
260 265 270

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Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln
 275 280 285

(2) INFORMATION FOR SEQ ID NO:168:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 290 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys
 1 5 10 15

Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro
 20 25 30

Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe
 35 40 45

Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp
 50 55 60

Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala Ala Arg
 65 70 75 80

Gln Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser
 85 90 95

Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr
 100 105 110

Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala
 115 120 125

Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu
 130 135 140

Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Glu Phe His Ala Tyr
 145 150 155 160

Val Glu Gly Gly Gly Ser Pro Gly Gly Ser Gly Gly Ser
 165 170 175

Asn Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
 180 185 190

Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu
 195 200 205

Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu
 210 215 220

Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu

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225	230	235	240
Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala			
245		250	255
Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe			
260		265	270
Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu			
275		280	285
Gln Gln			
290			

(2) INFORMATION FOR SEQ ID NO:169:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 45 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:169:

ACGTCCATGG CNTCNCCNGC NCCNCCTGCT TGTGACCTCC GAGTC

45

(2) INFORMATION FOR SEQ ID NO:170:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:170:

AATAGCTGAA TTCTTACCCCT TCCTGAGACA GATT

34

(2) INFORMATION FOR SEQ ID NO:171:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: other nucleic acid
 - (A) DESCRIPTION: /desc = "synthetic DNA"

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:

TGACAAGCTT ACCTGACGCA GAGGGTGGAC CCT

33

(2) INFORMATION FOR SEQ ID NO:172:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 30 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172:

ATGCACGAAT TCCCTGACGC AGAGGGTGGA

30

(2) INFORMATION FOR SEQ ID NO:173:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 14 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:173:

AATTCCATGC ATAC

14

(2) INFORMATION FOR SEQ ID NO:174:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

- (A) DESCRIPTION: /desc = "synthetic DNA"

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:174:

GGTACGTATG

10

(2) INFORMATION FOR SEQ ID NO:175:

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- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 561 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

ATGGCTCCAG TACCACCAAGG TGAAGATTCC AAAGATGTGG CCGCCCCACA CAGACAGCCA	60
CTCACCTCTT CAGAACGAAT TGACAAACAA ATTGGTACA TCCTCGACGG GATATCAGCC	120
CTGAGAAAGG AGACATGTAA CAAGAGTAAC ATGTGTGAAA GCAGCAAAGA GGCGCTAGCA	180
GAAAACAACC TGAACCTTCC AAAGATGGCT GAAAAAGATG GATGCTTCCA ATCCGGATTC	240
AATGAGGAGA CTTGCCTGGT GAAAATCATC ACTGGTCTTT TGGAGTTGA GGTATACCTC	300
GAGTACCTCC AGAACAGATT TGAGAGTAGT GAGGAACAAG CCAGAGCTGT GCAGATGTCG	360
ACAAAAGTCC TGATCCAGTT CCTGCAGAAA AAGGCAAAGA ATCTAGATGC AATAACCACC	420
CCTGACCCAA CCACAAATGC ATCCCTGCTG ACGAAGCTGC AGGCACAGAA CCAGTGGCTG	480
CAGGACATGA CAACTCATCT CATTCTGCAG AGCTTTAAGG AGTTCCCTGCA GTCCAGCCTG	540
AGGGCTCTTC GGCAAATGTA G	561

(2) INFORMATION FOR SEQ ID NO:176:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 402 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

ATGGCACCGG CTCGTTCCCC GTCCCCGTCT ACCCAGCCGT GGGAACACGT GAATGCCATC	60
CAGGAGGCCG GCGCTCTCCT GAACCTGAGT AGAGACACTG CTGCTGAGAT GAATGAAACA	120
GTAGAAGTGA TATCAGAAAT GTTGACCTC CAGGAGCCGA CTTGCCTACA GACCCGGCTG	180
GAGCTGTACA AGCAGGGCCT GCGGGGCAGC CTCACCAAGC TCAAGGGCCC CTTGACCATG	240
ATGGCCAGCC ACTACAAGCA GCACTGCCCT CCAACCCCGG AAACCTCCTG TGCAACCCAG	300
ATTATCACCT TTGAAAGTTT CAAAGAGAAC CTGAAGGACT TCCTGCTTGT CATCCCTTT	360
GACTGCTGGG AGCCAGTCCA GGAGTGATAA GGATCCGAAT TC	402

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(2) INFORMATION FOR SEQ ID NO:177:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 546 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:

ATGGCTACAC CATTAGGCC	TGCCAGCTCC CTGCCCCAGA	GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA	GGCGATGGC GCAGCGCTCC	AGGAGAAAGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCCGA	GGAGCTGGTG CTGCTCGGAC	ACTCTCTGGG CATCCCCTGG	180
GCTCCCTGA GCTCCTGCC	CAGCCAGGCC CTGCAGCTGG	CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTTCCTCTA	CCAGGGGCTC CTGCAGGCC	TGGAAGGGAT ATCCCCCGAG	300
TTGGGTCCA CCTTGGACAC	ACTGCAGCTG GACGTCGCCG	ACTTTGCCAC CACCATCTGG	360
CAGCAGATGG AAGAACTGGG	AATGGCCCT GCCCTGCAGC	CCACCCAGGG TGCCATGCCG	420
GCCTTCGCC	CTGCTTTCCA GCGCCGGGCA	GGAGGGTCC TGGTTGCTAG CCATCTGCAG	480
AGCTTCTGG AGGTGTCGTA	CCGCCTCTA CGCCACCTTG	CGCAGCCCTG ATAAGGATCC	540
GAATTC			546

(2) INFORMATION FOR SEQ ID NO:178:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 546 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

ATGGCTACAC CATTAGGACC	TGCCAGCTCC CTGCCCCAGA	GCTTCCTGCT CAAGTGCTTA	60
GAGCAAGTGA GGAAGATCCA	GGCGATGGC GCAGCGCTCC	AGGAGAAAGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCCGA	GGAGCTGGTG CTGCTCGGAC	ACTCTCTGGG CATCCCCTGG	180
GCTCCCTGA GCTCCTGCC	CAGCCAGGCC CTGCAGCTGG	CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTTCCTCTA	CCAGGGGCTC CTGCAGGCC	TGGAAGGGAT ATCCCCCGAG	300
TTGGGTCCA CCTTGGACAC	ACTGCAGCTG GACGTCGCCG	ACTTTGCCAC CACCATCTGG	360

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CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTCCA GCGCCGGCA GGAGGGTCC TGGTTGCTAG CCATCTGCAG	480
AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTG ATAAGGATCC	540
GAATT C	546

(2) INFORMATION FOR SEQ ID NO:179:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 546 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:

ATGGCTACAC CATTGGGCC TGCCAGCTCC CTGCCCCAGA GCTTCCTGCT CAAGTCTTTA	60
GAGCAAGTGA GGAAGATCCA GGGCGATGGC GCAGCGCTCC AGGAGAAGCT GTGTGCCACC	120
TACAAGCTGT GCCACCCGA GGAGCTGGTG CTGCTCGGAC ACTCTCTGGG CATCCCCTGG	180
GCTCCCTGA GCTCCTGCC CAGCCAGGCC CTGCAGCTGG CAGGCTGCTT GAGCCAACTC	240
CATAGCGGCC TTTTCCTCTA CCAGGGGCTC CTGCAGGCC TGGAAGGGAT ATCCCCGAG	300
TTGGGTCCCA CCTTGGACAC ACTGCAGCTG GACGTCGCCG ACTTTGCCAC CACCATCTGG	360
CAGCAGATGG AAGAACTGGG AATGGCCCCT GCCCTGCAGC CCACCCAGGG TGCCATGCCG	420
GCCTTCGCCT CTGCTTCCA GCGCCGGCA GGAGGGTCC TGGTTGCTAG CCATCTGCAG	480
AGCTTCCTGG AGGTGTCGTA CCGCGTTCTA CGCCACCTTG CGCAGCCCTG ATAAGGATCC	540
GAATT C	546

(2) INFORMATION FOR SEQ ID NO:180:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 465 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:

ATGGCGTCTC CGGCGCCGCC TGCTTGTGAC CTCCGAGTCC TCAGTAAACT GCTTCGTGAC	60
TCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCCAGAGG TTCACCCTT GCCTACACCT	120

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GTCCTGCTGC CTGCTGTGGA CTTTAGCTTG GGAGAATGGA AAACCCAGAT GGAGGGAGACC	180
AAGGCACAGG ACATTCTGGG AGCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG	240
GGACAACCTGG GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTCTGG ACAGGTCCGT	300
CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAAACCCAGC TTCCCTCCACA GGGCAGGACC	360
ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC AACACCTGCT CCGAGGAAAG	420
GTGCGTTTCC TGATGCTTGT AGGAGGGTCC ACCCTCTGCG TCAGG	465

(2) INFORMATION FOR SEQ ID NO:181:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 143 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

CCTGTCAACC CGGGCGGCCG CTCTGGTGGT GGTTCTGGTG GCGGCTCTGA GGGTGGCGGC	60
TCTGAGGGTG GCGGTTCTGA GGGTGGCGGC TCTGAGGGTG GCGGTTCCGG TGGCGGCTCC	120
GGTTCCGGTA ACATGTATTA TGA	143

(2) INFORMATION FOR SEQ ID NO:182:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 180 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:

ATCGTCTGAC CTCCCGGGCC TCCTGTCAAT GCTGGCGCG GCTCTGGTGG TGGTTCTGGT	60
GGCGGCTCTG AGGGTGGCGG CTCTGAGGGT GGCGGTTCTG AGGGTGGCGG CTCTGAGGGT	120
GGCGGTTCCG GTGGCGGCTC CGGTTCCGGT GATTTGATT ATGAAAACAT GTCAAACGCT	180

(2) INFORMATION FOR SEQ ID NO:183:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 858 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:183:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCAGCTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240
TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG ATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAATCGA GGGAAAGGATT	360
TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCGT CTCCGGCGCC GCCTGCTTGT	420
GACCTCCGAG TCCTCAGTAA ACTGCTTCGT GACTCCCAGT TCCTTCACAG CAGACTGAGC	480
CAGTGCCCAAG AGGTTCACCC TTTGCCTACA CCTGTCTGC TGCGCTGTGT GGACTTTAGC	540
TTGGGAGAAT GGAAAACCCA GATGGAGGAG ACCAAGGCAC AGGACATTCT GGGAGCAGTG	600
ACCCCTCTGC TGGAGGGAGT GATGGCAGCA CGGGGACAAC TGGGACCCAC TTGCCCTCTCA	660
TCCCTCCTGG GGCAGCTTTC TGGACAGGTC CGTCTCCTCC TTGGGGCCCT GCAGAGCCTC	720
CTTGGAACCC AGCTTCTCC ACAGGGCAGG ACCACAGCTC ACAAGGATCC CAATGCCATC	780
TTCCTGAGCT TCCAACACCT GCTCCGAGGA AAGGTGCGTT TCCTGATGCT TGTAGGAGGG	840
TCCACCCTCT GCGTCAGG	858

(2) INFORMATION FOR SEQ ID NO:184:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 858 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:184:

ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG ACCACCTAAC	60
CCTTTGCTGG ACCCGAACAA CCTCAATTCT GAAGACATGG ATATCCTGAT GGAACGAAAC	120
CTTCGAACTC CAAACCTGCT CGCATTGTA AGGGCTGTCA AGCAGCTTAGA AAATGCATCA	180
GGTATTGAGG CAATTCTCG TAATCTCAA CCATGTCTGC CCTCTGCCAC GGCGCACCC	240

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TCTCGACATC CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG	300
TTCTATCTGG TTACCCCTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG CGGTGGAGGC	360
TCCCCGGGTG GTGGTTCTGG CGGCCGGCTCC AACATGGCGT CTCCGGGCC GCCTGCTTGT	420
GACCTCCGAG TCCTCAGTAA ACTGCTTCGT GACTCCCAGT TCCTTCACAG CAGACTGAGC	480
CAGTGCCCAG AGGTTCACCC TTTGCCTACA CCTGTCCTGC TGCCTGCTGT GGACTTTAGC	540
TTGGGAGAAT GGAAAACCCA GATGGAGGAG ACCAAGGCAC AGGACATTCT GGGAGCAGTG	600
ACCCCTCTGC TGGAGGGAGT GATGGCAGCA CGGGGACAAC TGGGACCCAC TTGCTCTCA	660
TCCCTCCTGG GGCAGCTTTC TGGACAGGTC CGTCTCCTCC TTGGGGCCCT GCAGAGCCTC	720
CTTGGAACCC AGCTTCCTCC ACAGGGCAGG ACCACAGCTC ACAAGGATCC CAATGCCATC	780
TTCCTGAGCT TCCAACACCT GCTCCGAGGA AAGGTGCGTT TCCTGATGCT TGTAGGAGGG	840
TCCACCCCTCT GCGTCAGG	858

(2) INFORMATION FOR SEQ ID NO:185:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 852 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:185:

ATGGCGTCTC CGGCGCCGCC TGCTTGTGAC CTCCGAGTCC TCAGTAAACT GCTTCGTGAC	60
TCCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCCAGAGG TTCACCCCTT GCCTACACCT	120
GTCCCTGCTGC CTGCTGTGGA CTTTAGCTTG GGAGAATGGA AAACCCAGAT GGAGGAGACC	180
AAGGCACAGG ACATTCTGGG ACCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG	240
GGACAACCTGG GACCCACTTG CCTCTCATCC CTCCTGGGCC AGCTTCTGG ACAGGTCCGT	300
CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCCTCCACA GGGCAGGACC	360
ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC AACACCTGCT CCGAGGAAAG	420
GTGCGTTCC TGATGCTTGT AGGAGGGTCC ACCCTCTGCG TCAGGATCGA GGGAGGATT	480
TCCCCGGGTG GTGGTTCTGG CGGCCGGCTCC AACATGGCTA ACTGCTCTAT AATGATCGAT	540
GAAATTATAC ATCACTTAAA GAGACCACCT AACCCCTTGC TGGACCCGAA CAACCTCAAT	600
TCTGAAGACA TGGATATCCT GATGGAACGA AACCTTCGAA CTCCAAACCT GCTCGCATTG	660
GTAAGGGCTG TCAAGCACTT AGAAAATGCA TCAGGTATTG AGGCAATTCT TCGTAATCTC	720

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CAACCATGTC TGCCTCTGC CACGGCCGCA CCCTCTCGAC ATCCAATCAT CATCAAGGCA	780
GGTGAAGTGGC AAGAATTCCG GGAAAAACTG ACGTTCTATC TGGTTACCCCT TGAGCAAGCG	840
CAGGAACAAAC AG	852

(2) INFORMATION FOR SEQ ID NO:186:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 870 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

ATGGCGTCTC CGGCGCCGCC TGCTTGTGAC CTCCGAGTCC TCAGTAAACT GCTTCGTGAC	60
TCCCCATGTCC TTCACAGCAG ACTGAGCCAG TGCCCAGAGG TTCACCCCTT GCCTACACCT	120
GTCCTGCTGC CTGCTGTGGA CTTTAGCTTG GGAGAATGGA AAACCCAGAT GGAGGGAGACC	180
AAGGCACAGG ACATTCTGGG ACCAGTGACC CTTCTGCTGG AGGGAGTGAT GGCAGCACGG	240
GGACAACCTGG GACCCACTTG CCTCTCATCC CTCCTGGGGC AGCTTCTGG ACAGGTCCGT	300
CTCCTCCTTG GGGCCCTGCA GAGCCTCCTT GGAACCCAGC TTCCCTCCACA GGGCAGGACC	360
ACAGCTCACA AGGATCCCAA TGCCATCTTC CTGAGCTTCC AACACCTGCT CCGAGGAAAG	420
GTGCGTTCC TGATGCTTGT AGGAGGGTCC ACCCTCTGCG TCAGGGAAATT CCATGCATAC	480
GTAGAGGGCG GTGGAGGCTC CCCGGGTGGT GGTTCTGGCG GCGGCTCCAA CATGGCTAAC	540
TGCTCTATAA TGATCGATGA ATTATACAT CACTTAAAGA GACCACCTAA CCCTTGCTG	600
GACCCGAACA ACCTCAATTG TGAAGACATG GATATCCTGA TGGAACGAAA CCTTCGAAC	660
CCAAACCTGC TCGCATTGTC AAGGGCTGTC AAGCACTTAG AAAATGCATC AGGTATTGAG	720
GCAATTCTTC GTAATCTCCA ACCATGTCTG CCCTCTGCCA CGGCCGCACC CTCTCGACAT	780
CCAATCATCA TCAAGGCAGG TGACTGGCAA GAATTCCGGG AAAAACTGAC GTTCTATCTG	840
GTTACCCCTTG AGCAAGCGCA GGAACAAACAG	870

(2) INFORMATION FOR SEQ ID NO:187:

(i) SEQUENCE CHARACTERISTICS:-

- (A) LENGTH: 18 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:187:

Met Ser Arg Leu Pro Val Leu Leu Leu Gln Leu Leu Val Arg Pro
1 5 10 15

Ala Met

(2) INFORMATION FOR SEQ ID NO:188:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Asn

(2) INFORMATION FOR SEQ ID NO:189:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:

Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Gly Gly Ser Gly Gly Gly
 1 5 10 15

Ser Asn

(2) INFORMATION FOR SEQ ID NO:190:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 18 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:190:

Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Ser Gly Gly
1 5 10 15

Ser Asn

(2) INFORMATION FOR SEQ ID NO:191:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:191:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile
1 5 10 15

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25 30

Asn

(2) INFORMATION FOR SEQ ID NO:192:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192:

Tyr Val Ile Glu Gly Lys Ile Ser Pro Gly Glu Pro Ser Gly Pro Ile
1 5 10 15

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25 30

Asn

(2) INFORMATION FOR SEQ ID NO:193:

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- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile
1 5 10 15

Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro
20 25 30

Asn

(2) INFORMATION FOR SEQ ID NO:194:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 49 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:194:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gly Gly Ser Gly Gly Gly
1 5 10 15

Ser Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser Glu
20 25 30

Gly Gly Gly Ser Glu Gly Gly Ser Gly Gly Ser Gly Ser Gly
35 40 45

Asn

(2) INFORMATION FOR SEQ ID NO:195:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 60 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:195:

Tyr Val Ile Glu Gly Arg Ile Ser Pro Gln Pro Pro Val Asn Ala Gly
1 5 10 15

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Ser Gly Gly Ser
20 25 30

Glu Gly Gly Ser Glu Gly Gly Ser Glu Gly Gly Ser Gly
35 40 45

Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu Asn
50 55 60

(2) INFORMATION FOR SEQ ID NO:196:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:

Glu Phe His Ala Tyr Val Glu Gly Gly Ser Pro Gly Gly Gly
1 5 10 15

Ser Gly Gly Ser Asn
20

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WHAT IS CLAIMED IS:

1. A fusion protein having the formula selected from the group consisting of

5

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁
wherein R₁ is a human interleukin-3 mutant
polypeptide of the Formula:

10 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn

1 5 10 15

Cys Xaa Xaa

20 25 30

15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa Xaa

35 40 45

20

Xaa Xaa

50 55 60

Xaa Xaa

65 70 75

25

Xaa Xaa

80 85 90

30

Xaa Xaa

95 100 105

Xaa Phe Xaa Xaa

110 115 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe

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125

130

[SEQ ID NO:1]

wherein

- 5 Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or
Arg;
- Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
Gln;
- Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or
10 Cys;
- Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
Ala;
- Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
Gln, Asn, Thr, Ser or Val;
- 15 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp,
Asn, Gln, Leu, Val or Gly;
- Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
Phe, Leu, Ser, or Arg;
- Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or
20 Leu;
- Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
- Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or
Trp;
- 25 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
- Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
Trp;
- Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
- Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,
30 Leu, or Lys;
- Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or
Gln;
- Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
or Glu;

Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;
Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
Thr, Arg, Ala, Phe, Ile or Met;
Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or
5 Val;
Xaa at position 36 is Asp, Leu, or Val;
Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;
Xaa at position 38 is Asn, or Ala;
Xaa at position 40 is Leu, Trp, or Arg;
10 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or
Pro;
Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr,
Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala;
Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
15 Cys, Gln, Arg, Thr, Gly or Ser;
Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
Trp, Glu, Asn, Gln, Ala or Pro;
Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;
20 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,
Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or
His;
Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe,
25 Glu, Lys, Thr, Ala, Met, Val or Asn;
Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
or Asp;
Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,
Ser, Ala, Ile, Val, His, Phe, Met or Gln;
30 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or
Thr;
Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,

- Ser, or Met;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
Asn, Lys, His, Ala or Leu;
- Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- 5 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,
His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 57 is Asn or Gly;
- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or
Cys;
- 10 Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg;
Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;
Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or
Ser;
- Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or
15 Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro,
or Val;
- Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or
20 Ser;
- Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or
Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
Pro, or His;
- 25 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr,
or His;
- Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp,
Gly, or Leu;
- Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 30 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr,
Gln, Trp, or Asn;
- Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg,
or Asp;
- Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,

- or Arg;
- Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,
Ser, Gln, or Leu;
- 5 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro;
Gly, or Asp;
Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or
Arg;
- 10 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly,
or Asp;
Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
or Arg;
Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
- 15 or Lys;
Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- 20 Xaa at position 85 is Leu, Asn, Val, or Gln;
Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
Xaa at position 87 is Leu, Ser, Trp, or Gly;
Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
- 25 Asn, or Ser;
Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;
Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;
- 30 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;
Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
- Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln,

Lys, His, Ala, or Pro;

Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;

Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

5 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;

Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;

Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;

10 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
Gln, or Pro;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;

Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
15 Pro;

Xaa at position 103 is Asp, or Ser;

Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;

Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
20 Tyr, Leu, Lys, Ile, Asp, or His;

Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;

Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,
His, Ser, Ala or Pro;

25 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
or Gly;

Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln,
His, Glu, Ser, Ala, or Trp;

Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;

30 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser,
or Phe;

Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
Asp, Lys, Leu, Ile, Val or Asn;

Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or

Leu;

Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His,
Thr, Trp, or Met;

Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val,
5 Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or
Ile;

Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or
Pro;

Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
10 or Tyr;

Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
or Arg;

Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or
Gln;

15 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
20 or Leu;

and which can additionally have Met- preceding the amino acid in
position 1; and wherein from 1 to 14 amino acids can be deleted
from the N-terminus and/or from 1 to 15 amino acids can be deleted
25 from the C-terminus; and wherein from 4 to 44 of the amino acids
designated by Xaa are different from the corresponding amino acids
of native (1-133) human interleukin-3;

R₂ is a IL-3, IL-3 variant or a colony stimulating factor,
30 and

L is a linker capable of linking R₁ to R₂.

2. The fusion protein of claim 1 wherein said colony

stimulating factor is selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, 5 human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF)

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3. The fusion protein of claim 2 wherein R₁ is of the Formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
5 1 5 10 .. 15

Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa Xaa
20 . 25 . 30

10 Xaa Xaa Xaa Xaa Kaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa Xaa
35 . 40 . 45

Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu Xaa
50 . 55 . 60

15 Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile Glu
65 . 70 . 75

Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr Ala
20 80 . 85 . 90

Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa Xaa
95 . 100 . 105

25 Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Leu Glu Xaa
110 . 115 . 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
125 . 130

30 [SEQ ID NO:2]

wherein

Xaa at position 17 is Ser, Gly, Asp, Met, or Gln;
Xaa at position 18 is Asn, His, or Ile;

Xaa at position 19 is Met or Ile;
Xaa at position 21 is Asp or Glu;
Xaa at position 23 is Ile, Ala, Leu, or Gly;
Xaa at position 24 is Ile, Val, or Leu;
5 Xaa at position 25 is Thr, His, Gln, or Ala;
Xaa at position 26 is His or Ala;
Xaa at position 29 is Gln, Asn, or Val;
Xaa at position 30 is Pro, Gly, or Gln;
Xaa at position 31 is Pro, Asp, Gly, or Gln;
10 Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or
Glu;
Xaa at position 33 is Pro or Glu;
Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
Gln, Glu, Ile, Phe, Thr or Met;
15 Xaa at position 35 is Leu, Ala, Asn, Pro, Gln, or Val;
Xaa at position 37 is Phe, Ser, Pro, or Trp;
Xaa at position 38 is Asn or Ala;
Xaa at position 42 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
Leu, Met, Tyr or Arg;
20 Xaa at position 44 is Asp or Glu;
Xaa at position 45 is Gln, Val, Met, Leu, Thr, Ala, Asn,
Glu, Ser or Lys;
Xaa at position 46 is Asp, Phe, Ser, Thr, Ala, Asn Gln,
Glu, His, Ile, Lys, Tyr, Val or Cys;
25 Xaa at position 50 is Glu, Ala, Asn, Ser or Asp;
Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
Xaa at position 54 is Arg or Ala;
Xaa at position 55 is Arg, Thr, Val, Leu, or Gly;
30 Xaa at position 56 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val or Lys;
Xaa at position 60 is Ala or Ser;
Xaa at position 62 is Asn, Pro, Thr, or Ile;
Xaa at position 63 is Arg or Lys;

- Xaa at position 64 is Ala or Asn;
Xaa at position 65 is Val or Thr;
Xaa at position 66 is Lys or Arg;
Xaa at position 67 is Ser, Phe, or His;
5 Xaa at position 68 is Leu, Ile, Phe, or His;
Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
Xaa at position 71 is Ala, Pro, or Arg;
Xaa at position 72 is Ser, Glu, Arg, or Asp;
10 Xaa at position 73 is Ala or Leu;
Xaa at position 76 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
Xaa at position 77 is Ile or Leu;
Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
15 Gly, or Asp;
Xaa at position 80 is Asn, Gly, Glu, or Arg;
Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
Xaa at position 83 is Pro or Thr;
20 Xaa at position 85 is Leu or Val;
Xaa at position 87 is Leu or Ser;
Xaa at position 88 is Ala or Trp;
Xaa at position 91 is Ala or Pro;
Xaa at position 93 is Thr, Asp, Ser, Pro, Ala, Leu, or
25 Arg;
Xaa at position 95 is His, Pro, Arg, Val, Leu, Gly, Asn,
Phe, Ser or Thr;
Xaa at position 96 is Pro or Tyr;
Xaa at position 97 is Ile or Val;
30 Xaa at position 98 is His, Ile, Asn, Leu, Ala, Thr, Leu,
Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
Xaa at position 99 is Ile, Leu, or Val;
Xaa at position 100 is Lys, Arg, Ile, Gln, Pro, or Ser;
Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Pro,

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- Asn, Ile, Leu or Tyr;
Xaa at position 104 is Trp or Leu;
Xaa at position 105 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
Leu, Lys, Ile, Asp, or His;
5 Xaa at position 106 is Glu or Gly;
Xaa at position 108 is Arg, Ala, or Ser;
Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
Xaa at position 112 is Thr, Val, or Gln;
Xaa at position 114 is Tyr or Trp;
10 Xaa at position 115 is Leu or Ala;
Xaa at position 116 is Lys, Thr, Val, Trp, Ser, Ala, His,
Met, Phe, Tyr or Ile;
Xaa at position 117 is Thr or Ser;
Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
15 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Asp, or
Gly;
Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;
Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr,
20 or Leu;

and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and wherein from 4 to 35 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133)human interleukin-3.

- 30 4. The fusion protein of claim 3 wherein R₁ is of the Formula:

Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn

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Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa Xaa
20 25 30

5 Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp Xaa
35 40 45

Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu Ala
50 55 60

10 Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile Glu
65 70 75

Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr Ala
15 80 85 90

Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Xaa Gly Asp Trp Xaa
95 100 105

20 Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu Xaa
110 115 120

Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
125 130

25 [SEQ ID NO:3]

wherein

Xaa at position 17 is Ser, Gly, Asp, or Gln;

Xaa at position 18 is Asn, His, or Ile;

30 Xaa at position 23 is Ile, Ala, Leu, or Gly;

Xaa at position 25 is Thr, His, or Gln;

Xaa at position 26 is His or Ala;

Xaa at position 29 is Gln or Asn;

Xaa at position 30 is Pro or Gly;

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- Xaa at position 32 is Leu, Arg, Asn, or Ala;
- Xaa at position 34 is Leu, Val, Ser, Ala, Arg, Gln, Glu, Ile, Phe, Thr, or Met;
- Xaa at position 35 is Leu, Ala, Asn, or Pro;
- 5 Xaa at position 38 is Asn or Ala;
- Xaa at position 42 is Gly, Asp, Ser, Ala, Asn, Ile, Leu, Met, Tyr or Arg;
- Xaa at position 45 is Gln, Val, Met, Leu, Ala, Asn, Glu, or Lys;
- 10 Xaa at position 46 is Asp, Phe, Ser, Gln, Glu, His, Val or Thr;
- Xaa at position 50 is Glu Asn, Ser or Asp;
- Xaa at position 51 is Asn, Arg, Pro, Thr, or His;
- Xaa at position 55 is Arg, Leu, or Gly;
- 15 Xaa at position 56 is Pro, Gly, Ser, Ala, Asn, Val, Leu or Gln;
- Xaa at position 62 is Asn, Pro, or Thr;
- Xaa at position 64 is Ala or Asn;
- Xaa at position 65 is Val or Thr;
- 20 Xaa at position 67 is Ser or Phe;
- Xaa at position 68 is Leu or Phe;
- Xaa at position 69 is Gln, Ala, Glu, or Arg;
- Xaa at position 76 is Ser, Val, Asn, Pro, or Gly;
- Xaa at position 77 is Ile or Leu;
- 25 Xaa at position 79 is Lys, Gly, Asn, Met, Arg, Ile, or Gly;
- Xaa at position 80 is Asn, Gly, Glu, or Arg;
- Xaa at position 82 is Leu, Gln, Trp, Arg, Asp, Asn, Glu, His, Met, Phe, Ser, Thr, Tyr or Val;
- 30 Xaa at position 87 is Leu or Ser;
- Xaa at position 88 is Ala or Trp;
- Xaa at position 91 is Ala or Pro;
- Xaa at position 93 is Thr, Asp, or Ala;
- Xaa at position 95 is His, Pro, Arg, Val, Gly, Asn, Ser or

Thr;

- Xaa at position 98 is His, Ile, Asn, Ala, Thr, Gln, Glu,
Lys, Met, Ser, Tyr, Val or Leu;
- Xaa at position 99 is Ile or Leu;
- 5 Xaa at position 100 is Lys or Arg;
- Xaa at position 101 is Asp, Pro, Met, Lys, Thr, His, Prc,
Asn, Ile, Leu or Tyr;
- Xaa at position 105 is Asn, Pro, Ser, Ile or Asp;
- Xaa at position 108 is Arg, Ala, or Ser;
- 10 Xaa at position 109 is Arg, Thr, Glu, Leu, or Ser;
- Xaa at position 112 is Thr or Gln;
- Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, Tyr
or Ile;
- Xaa at position 117 is Thr or Ser;
- 15 Xaa at position 120 is Asn, Pro, Leu, His, Val, or Gln;
- Xaa at position 121 is Ala, Ser, Ile, Pro, or Asp;
- Xaa at position 122 is Gln, Met, Trp, Phe, Pro, His, Ile,
or Tyr;
- Xaa at position 123 is Ala, Met, Glu, Ser, or Leu;
- 20 and which can additionally have Met- preceding the amino acid in position 1; and wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus; and wherein from 4
25 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133) human interleukin-3.

5. The fusion protein of claim 4 wherein R1
30 is of the Formula:

- Xaa at position 42 is Gly, Asp, Ser, Ile, Leu, Met, Tyr,
or Ala;
- 35 Xaa at position 45 is Gln, Val, Met or Asn;

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Xaa at position 46 is Asp, Ser, Gln, His or Val;
Xaa at position 50 is Glu or Asp;
Xaa at position 51 is Asn, Pro or Thr;
Xaa at position 62 is Asn or Pro;
5 Xaa at position 76 is Ser, or Pro;
Xaa at position 82 is Leu, Trp, Asp, Asn Glu, His, Phe,
Ser or Tyr;
Xaa at position 95 is His, Arg, Thr, Asn or Ser;
Xaa at position 98 is His, Ile, Leu, Ala, Gln, Lys, Met,
10 Ser, Tyr or Val;
Xaa at position 100 is Lys or Arg;
Xaa at position 101 is Asp, Pro, His, Asn, Ile or Leu;
Xaa at position 105 is Asn, or Pro;
Xaa at position 108 is Arg, Ala, or Ser;
15 Xaa at position 116 is Lys, Val, Trp, Ala, His, Phe, or
Tyr;
Xaa at position 121 is Ala, or Ile;
Xaa at position 122 is Gln, or Ile; and
Xaa at position 123 is Ala, Met or Glu.

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6. A fusion protein having the formula selected from
the group consisting of

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁
25 wherein R₁ is a human interleukin-3 mutant
polypeptide of the Formula:

Asn Cys Xaa Xaa

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Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa

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Xaa Xaa

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Xaa Xaa

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Xaa Xaa

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70

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Xaa Xaa

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Xaa Xaa Phe Xaa Xaa

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15 Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:4]

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wherein

- Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;
20 Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
Xaa at position 6 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
Xaa at position 7 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,
Gln, Asn, Thr, Ser or Val;
25 Xaa at position 8 is Glu, Trp, Pro, Ser, Ala, His, Asp,
Asn, Gln, Leu, Val, or Gly;
Xaa at position 9 is Ile, Val, Ala, Leu, Gly, Trp, Lys,
Phe, Leu, Ser, or Arg;
Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or
30 Leu;
Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
Xaa at position 12 is His, Thr, Phe, Gly, Arg, Ala, or
Trp;

Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala;
Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
Trp;
Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val;
5 Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser,
Leu, or Lys;
Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or
Gln;
Xaa at position 18 is Leu, Val, Arg, Gln, Asn, Gly, Ala,
10 or Glu;
Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu;
Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln,
Thr, Arg, Ala, Phe, Ile or Met;
Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or
15 Val;
Xaa at position 22 is Asp, Leu, or Val;
Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile;
Xaa at position 24 is Asn, or Ala;
Xaa at position 26 is Leu, Trp, or Arg;
20 Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro;
Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn,
Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met;
Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
Cys, Gln, Arg, Thr, Gly or Ser;
25 Xaa at position 30 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
Trp, Glu, Asn, Gln, Ala or Pro;
Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr,
Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp;
Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,
30 Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;
Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or
His;
Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe,
Glu, Lys, Thr, Ala, Met, Val or Asn;

- Xaa at position 35 is Met, Arg, Ala, Gly, Pro, Asn, His,
or Asp;
- Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,
Ser, Ala, Ile, Val, His, Phe, Met or Gln;
- 5 Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
- Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or
Thr;
- Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,
10 Ser, Met, or;
- Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
Asn, Lys, His, Ala or Leu;
- Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly;
- Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,
15 His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;
- Xaa at position 43 is Asn or Gly;
- Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or
Cys;
- Xaa at position 45 is Glu Tyr, His, Leu, Pro, or Arg;
- 20 Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- Xaa at position 47 is Phe, Asn, Glu, Pro, Lys, Arg, or
Ser;
- Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp,
or Ile;
- 25 Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, His, Pro,
or Val;
- Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys;
- Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, or
Ser;
- 30 Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or
Ser;
- Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
Pro, or His;
- Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr,

or His;

Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp,
Gly, or Leu;

Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;

5 Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr,
Gln, Trp, or Asn;

Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg,
or Asp;

Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,
10 or Arg;

Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;

Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,
Ser, Gln, or Leu;

Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro,
15 Gly, or Asp;

Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu;

Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or
Arg;

Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
20 or Asp;

Xaa at position 66 is Asn, Trp, Val, Gly, Thr, Leu, Glu,
or Arg;

Xaa at position 67 is Leu, Gln, Gly, Ala, Trp, Arg, Val,
or Lys;

25 Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,
Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;

Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;

Xaa at position 71 is Leu, Asn, Val, or Gln;

30 Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 73 is Leu, Ser, Trp, or Gly;

Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His,
Asn, or Ser;

- Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile,
or Met;
- Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp,
or His;
- 5 Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala,
Gly, Ile or Leu;
- Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;
- Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln,
10 Lys, His, Ala or Pro;
- Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly,
Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;
- Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;
- 15 Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr,
Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
Gly, Ser, Phe, or His;
- Xaa at position 86 is Lys, Tyr, Leu, His, Arg, Ile, Ser,
20 Gln, Pro;
- Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;
- Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or
Pro;
- 25 Xaa at position 89 is Asp, or Ser;
- Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;
- Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
Tyr, Leu, Lys, Ile, Asp, or His;
- 30 Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;
- Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,
His, Ser, Ala, or Pro;
- Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,

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or Gly;

Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg,
His, Glu, Ser, Ala or Trp;

Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;

5 Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser,
or Phe;

Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr,
Asp, Lys, Leu, Ile, Val or Asn;

10 Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or
Leu;

Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His,
Thr, Trp, or Met;

15 Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val,
Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or
Ile;

Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or
Pro;

Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp,
or Tyr;

20 Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr,
or Arg;

Xaa at position 106 is Asn, Ala, Pro, Leu, His, Val, or
Gln;

25 Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Lys, Asp,
or Gly;

Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
His, Ile, Tyr, or Cys;

Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

30

and which can additionally have Met- or Met-Ala- preceding
the amino acid in position 1; and wherein from 4 to 44 of
the amino acids designated by Xaa are different from the
corresponding native amino acids of (1-133) human

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interleukin-3;

R₂ is a colony stimulating factor; and

L is a linker capable of linking R₁ to R₂.

5

7. The fusion protein of claim 6 wherein said colony stimulating factor is selected from the group consisting of GM-CSF, CSF-1, G-CSF, Meg-CSF (more recently referred to as c-mpl ligand), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, LIF, flt3/flk2, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF)

15

8. The fusion protein of claim 7 wherein R₁ is of the formula:

20 Asn Cys Xaa Xaa Xaa Ile Xaa Glu Xaa Xaa Xaa Xaa Leu Lys Xaa
1 5 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Asp Xaa Xaa Asn Leu Asn Xaa Glu Xaa
20 25 30

25 Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Xaa Xaa Xaa Asn Leu Glu
35 40 45

30 Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Ile
50 55 60

Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Xaa Cys Xaa Pro Xaa Xaa Thr
65 70 75

35 Ala Xaa Pro Xaa Arg Xaa Xaa Xaa Xaa Xaa Gly Asp Xaa

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Xaa Xaa Phe Xaa Xaa Lys Leu Xaa Phe Xaa Xaa Xaa Xaa Leu Glu

5

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Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:5]

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10 wherein

Xaa at position 3 is Ser, Gly, Asp, Met, or Gln;

Xaa at position 4 is Asn, His, or Ile;

Xaa at position 5 is Met or Ile;

Xaa at position 7 is Asp or Glu;

15 Xaa at position 9 is Ile, Ala, Leu, or Gly;

Xaa at position 10 is Ile, Val, or Leu;

Xaa at position 11 is Thr, His, Gln, or Ala;

Xaa at position 12 is His or Ala;

Xaa at position 15 is Gln, Asn, or Val;

20 Xaa at position 16 is Pro, Gly, or Gln;

Xaa at position 17 is Pro, Asp, Gly, or Gln;

Xaa at position 18 is Leu, Arg, Gln, Asn, Gly, Ala, or
Glu;

Xaa at position 19 is Pro or Glu;

25 Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Ala, Arg,
Gln, Glu, Ile, Phe, Thr or Met;

Xaa at position 21 is Leu, Ala, Asn, Pro, Gln, or Val;

Xaa at position 23 is Phe, Ser, Pro, or Trp;

Xaa at position 24 is Asn or Ala;

30 Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Asn, Ile,
Leu, Met Tyr or Arg;

Xaa at position 30 is Asp or Glu;

Xaa at position 31 is Gln, Val, Met, Leu, Thr, Ala, Asn,
Glu, Ser or Lys;

- Xaa at position 32 is Asp, Phe, Ser, Thr, Ala, Asn, Gln,
Glu, His, Ile, Lys, Tyr, Val or Cys;
- Xaa at position 36 is Glu, Ala, Asn, Ser or Asp;
- Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or
5 His;
- Xaa at position 40 is Arg or Ala;
- Xaa at position 41 is Arg, Thr, Val, Leu, or Gly;
- Xaa at position 42 is Pro, Gly, Ser, Gln, Ala, Arg, Asn,
Glu, Leu, Thr, Val Or Lys;
- 10 Xaa at position 46 is Ala or Ser;
- Xaa at position 48 is Asn, Pro, Thr, or Ile;
- Xaa at position 49 is Arg or Lys;
- Xaa at position 50 is Ala or Asn;
- Xaa at position 51 is Val or Thr;
- 15 Xaa at position 52 is Lys or Arg;
- Xaa at position 53 is Ser, Phe, or His;
- Xaa at position 54 is Leu, Ile, Phe, or His;
- Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, or
Gly;
- 20 Xaa at position 57 is Ala, Pro, or Arg;
- Xaa at position 58 is Ser, Glu, Arg, or Asp;
- Xaa at position 59 is Ala or Leu;
- Xaa at position 62 is Ser, Val, Ala, Asn, Glu, Pro, or
Gly;
- 25 Xaa at position 63 is Ile or Leu;
- Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile,
Gly, or Asp;
- Xaa at position 66 is Asn, Gly, Glu, or Arg;
- Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Ala, Asn,
30 Glu, His, Ile, Met, Phe, Ser, Thr, Tyr or Val;
- Xaa at position 69 is Pro or Thr;
- Xaa at position 71 is Leu or Val;
- Xaa at position 73 is Leu or Ser;
- Xaa at position 74 is Ala or Trp;

- Xaa at position 77 is Ala or Pro;
- Xaa at position 79 is Thr, Asp, Ser, Pro, Ala, Leu, or Arg;
- Xaa at position 81 is His, Pro, Arg, Val, Leu, Gly, Asn,
5 Phe, Ser or Thr;
- Xaa at position 82 is Pro or Tyr;
- Xaa at position 83 is Ile or Val;
- Xaa at position 84 is His, Ile, Asn, Leu, Ala, Thr, Leu,
Arg, Gln, Leu, Lys, Met, Ser, Tyr, Val or Pro;
- 10 Xaa at position 85 is Ile, Leu, or Val;
- Xaa at position 86 is Lys, Arg, Ile, Gln, Pro, or Ser;
- Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Asn,
Ile, Leu or Tyr;
- Xaa at position 90 is Trp or Leu;
- 15 Xaa at position 91 is Asn, Pro, Ala, Ser, Trp, Gln, Tyr,
Leu, Lys, Ile, Asp, or His;
- Xaa at position 92 is Glu, or Gly;
- Xaa at position 94 is Arg, Ala, or Ser;
- Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
- 20 Xaa at position 98 is Thr, Val, or Gln;
- Xaa at position 100 is Tyr or Trp;
- Xaa at position 101 is Leu or Ala;
- Xaa at position 102 is Lys, Thr, Val, Trp, Ser, Ala, His,
Met, Phe, Tyr or Ile;
- 25 Xaa at position 103 is Thr or Ser;
- Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
- Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Asp, or
Gly;
- Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,
30 His, Ile, Tyr, or Cys;
- Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr,
or Leu;

which can additionally have Met- or Met-Ala- preceding the

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amino acid in position 1; and wherein from 4 to 35 of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3.

5 9. The fusion protein of claim 8 wherein R1 is of the formula:

Asn Cys Xaa Xaa Met Ile Asp Glu Xaa Ile Xaa Xaa Leu Lys Xaa
10 1 5 10 15

Xaa Pro Xaa Pro Xaa Xaa Asp Phe Xaa Asn Leu Asn Xaa Glu Asp
20 25 30

15 Xaa Xaa Ile Leu Met Xaa Xaa Asn Leu Arg Xaa Xaa Asn Leu Glu
35 40 45

Ala Phe Xaa Arg Xaa Xaa Lys Xaa Xaa Xaa Asn Ala Ser Ala Ile
50 55 60
20

Glu Xaa Xaa Leu Xaa Xaa Leu Xaa Pro Cys Leu Pro Xaa Xaa Thr
65 70 75

25 Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Xaa Xaa Gly Asp Trp
80 85 90

Xaa Glu Phe Xaa Xaa Lys Leu Xaa Phe Tyr Leu Xaa Xaa Leu Glu
95 100 105

30 Xaa Xaa Xaa Xaa Gln Gln [SEQ ID NO:6]
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wherein

Xaa at position 3 is Ser, Gly, Asp, or Gln;

Xaa at position 4 is Asn, His, or Ile;

35 Xaa at position 9 is Ile, Ala, Leu, or Gly;

- Xaa at position 11 is Thr, His, or Gln;
Xaa at position 12 is His or Ala;
Xaa at position 15 is Gln or Asn;
Xaa at position 16 is Pro or Gly;
5 Xaa at position 18 is Leu, Arg, Asn, or Ala;
Xaa at position 20 is Leu, Val, Ser, Ala, Arg, Gln, Glu,
Ile, Phe, Thr or Met;
Xaa at position 21 is Leu, Ala, Asn, or Pro;
Xaa at position 24 is Asn or Ala;
10 Xaa at position 28 is Gly, Asp, Ser, Ala, Asn, Ile, Leu,
Met, Tyr or Arg;
Xaa at position 31 is Gln, Val, Met, Leu, Ala, Asn, Glu or
Lys;
Xaa at position 32 is Asp, Phe, Ser, Ala, Gln, Glu, His,
15 Val or Thr;
Xaa at position 36 is Glu, Asn, Ser or Asp;
Xaa at position 37 is Asn, Arg, Pro, Thr, or His;
Xaa at position 41 is Arg, Leu, or Gly;
Xaa at position 42 is Pro, Gly, Ser, Ala, Asn, Val, Leu or
20 Gln;
Xaa at position 48 is Asn, Pro, or Thr;
Xaa at position 50 is Ala or Asn;
Xaa at position 51 is Val or Thr;
Xaa at position 53 is Ser or Phe;
25 Xaa at position 54 is Leu or Phe;
Xaa at position 55 is Gln, Ala, Glu, or Arg;
Xaa at position 62 is Ser, Val, Asn, Pro, or Gly;
Xaa at position 63 is Ile or Leu;
Xaa at position 65 is Lys, Asn, Met, Arg, Ile, or Gly;
30 Xaa at position 66 is Asn, Gly, Glu, or Arg;
Xaa at position 68 is Leu, Gln, Trp, Arg, Asp, Asn, Glu,
His, Met, Phe, Ser, Thr, Tyr or Val;
Xaa at position 73 is Leu or Ser;
Xaa at position 74 is Ala or Trp;

Xaa at position 77 is Ala or Pro;
Xaa at position 79 is Thr, Asp, or Ala;
Xaa at position 81 is His, Pro, Arg, Val, Gly, Asn, Ser or
Thr;

5 Xaa at position 84 is His, Ile, Asn, Ala, Thr, Arg, Gln,
Glu, Lys, Met, Ser, Tyr, Val or Leu;
Xaa at position 85 is Ile or Leu;
Xaa at position 86 is Lys or Arg;
Xaa at position 87 is Asp, Pro, Met, Lys, His, Pro, Asn,
10 Ile, Leu or Tyr;

Xaa at position 91 is Asn, Pro, Ser, Ile or Asp;
Xaa at position 94 is Arg, Ala, or Ser;
Xaa at position 95 is Arg, Thr, Glu, Leu, or Ser;
Xaa at position 98 is Thr or Gln;

15 Xaa at position 102 is Lys, Val, Trp, or Ile;
Xaa at position 103 is Thr, Ala, His, Phe, Tyr or Ser;
Xaa at position 106 is Asn, Pro, Leu, His, Val, or Gln;
Xaa at position 107 is Ala, Ser, Ile, Pro, or Asp;
Xaa at position 108 is Gln, Met, Trp, Phe, Pro, His, Ile,
20 or Tyr;

Xaa at position 109 is Ala, Met, Glu, Ser, or Leu;

and which can additionally have Met- or Met-Ala- preceding
the amino acid in position 1; and wherein from 4 to 26 of
25 the amino acids designated by Xaa are different from the
corresponding amino acids of native (1-133)human
interleukin-3.

10. The fusion protein of claim 9 wherein R₁
30 is of the formula:

Xaa at position 17 is Ser, Lys, Asp, Met, Gln, or Arg;
Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or
35 Gln;

- Xaa at position 19 is Met, Arg, Gly, Ala, or Cys;
- Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or
Ala;
- Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, or
5 Val;
- Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, or
Gly;
- Xaa at position 23 is Ile, Ala, Gly, Trp, Lys, Leu, Ser,
or Arg;
- 10 Xaa at position 24 is Ile, Gly, Arg, or Ser;
- Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or
Ala;
- Xaa at position 26 is His, Thr, Phe, Gly, Ala, or Trp;
- Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
- 15 Xaa at position 28 is Lys, Leu, Gln, Gly, Pro, Val or Trp;
- Xaa at position 29 is Gln, Asn, Pro, Arg, or Val;
- Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser,
Leu, or Lys;
- Xaa at position 31 is Pro, Asp, Gly, Arg, Leu, or Gln;
- 20 Xaa at position 32 is Leu, Arg, Gln, Asn, Gly, Ala, or
Glu;
- Xaa at position 33 is Pro, Leu, Gln, Thr, or Glu;
- Xaa at position 34 is Leu, Gly, Ser, or Lys;
- Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, or Gln;
- 25 Xaa at position 36 is Asp, Leu, or Val;
- Xaa at position 37 is Phe, Ser, or Pro;
- Xaa at position 38 is Asn, or Ala;
- Xaa at position 40 is Leu, Trp, or Arg;
- Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, Pro;
- 30 Xaa at position 42 is Gly, Asp, Ser, Cys, or Ala;
- Xaa at position 42 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,
Cys, or Ser;
- Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,
Trp, or Pro;

- Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,
Lys, or Trp;
- Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, or Gly;
- Xaa at position 47 is Ile, Gly, Ser, Arg, Pro, or His;
- 5 Xaa at position 48 is Leu, Ser, Cys, Arg, His, Phe, or
Asn;
- Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His,
or Asp;
- Xaa at position 50 is Glu, Leu, Thr, Asp, or Tyr;
- 10 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or
His;
- Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or
Thr;
- Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,
15 Ser, or;
- Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,
or Leu;
- Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;
- Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, or Lys;
- 20 Xaa at position 57 is Asn or Gly;
- Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or
Cys;
- Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
- Xaa at position 60 is Ala, Ser, Tyr, Asn, or Thr;
- 25 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or
Ser;
- Xaa at position 62 is Asn His, Val, Arg, Pro, Thr, or Ile;
- Xaa at position 63 is Arg, Tyr, Trp, Ser, Pro, or Val;
- Xaa at position 64 is Ala, Asn, Ser, or Lys;
- 30 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or
Ser;
- Xaa at position 66 is Lys, Ile, Val, Asn, Glu, or Ser;
- Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile,
Pro, or His;

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- Xaa at position 68 is Leu, Val, Trp, Ser, Thr, or His;
Xaa at position 69 is Gln, Ala, Pro, Thr, Arg, Trp, Gly,
or Leu;
- Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 5 Xaa at position 71 is Ala, Met, Leu, Arg, Glu, Thr, Gln,
Trp, or Asn;
- Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg,
or Asp;
- Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr,
10 or Arg;
- Xaa at position 74 is Ile, Thr, Pro, Arg, Gly, Ala;
- Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,
Ser, or Leu;
- Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro,
15 Gly, or Asp;
- Xaa at position 77 is Ile, Ser, Arg, or Thr;
- Xaa at position 78 is Leu, Ala, Ser, Glu, Gly, or Arg;
- Xaa at position 79 is Lys, Thr, Gly, Asn, Met, Ile, or
Asp;
- 20 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, or
Arg;
- Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, or
Lys;
- Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, or Asp;
- 25 Xaa at position 83 is Pro, Thr, Trp, Arg, or Met;
- Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- Xaa at position 85 is Leu, Asn, or Gln;
- Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
- Xaa at position 87 is Leu, Ser, Trp, or Gly;
- 30 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
- Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His,
or Asn;
- Xaa at position 90 is Ala, Ser, Asp, Ile, or Met;
- Xaa at position 91 is Ala, Ser, Thr, Phe, Leu, Asp, or

His;

Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, or
Leu;

5 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu,
or Arg;

Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, or
Pro;

Xaa at position 95 is His, Gln, Pro, Val, Leu, Thr or Tyr;

Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

10 Xaa at position 97 is Ile, Lys, Ala, or Asn;

Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
or Pro;

Xaa at position 99 is Ile, Arg, Asp, Pro, Gln, Gly, Phe,
or His;

15 Xaa at position 100 is Lys, Tyr, Leu, His, Ile, Ser, Gln,
or Pro;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
Tyr, or Gln;

20 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or
Pro;

Xaa at position 103 is Asp, or Ser;

Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,
Leu, Gln, Lys, Ala, Phe, or Gly;

25 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,
Tyr, Leu, Lys, Ile, or His;

Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly,
or Pro;

Xaa at position 108 is Arg, Asp, Leu, Thr, Ile, or Pro;

30 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser,
or Gly.

11. The fusion protein of claim 10 wherein
R1 is of the Formula:

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	1	5	10
	(Met) _m -Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr		
	15	20	
	Ser Trp Val Asn Cys Ser Xaa Xaa Xaa Asp Glu Ile Ile		
5	25	30	35
	Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa		
	40	45	50
	Xaa Asn Leu Asn Xaa Glu Asp Xaa Asp Ile Leu Xaa Glu		
	55	60	
10	Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa		
	65	70	75
	Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa		
	80	85	
	Ile Leu Xaa Asn Leu Xaa Pro Cys Xaa Pro Xaa Xaa Thr		
15	90	95	100
	Ala Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly		
	105	110	115
	Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu		
	120	125	
20	Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln Thr Thr Leu		
	130		
	Ser Leu Ala Ile Phe [SEQ ID NO:7]		

wherein m is 0 or 1; Xaa at position 18 is Asn or Ile; Xaa at position 19 is Met, Ala or Ile; Xaa at position 20 is Ile, Pro or Ile; Xaa at position 23 is Ile, Ala or Leu; Xaa at position 25 is Thr or His; Xaa at position 29 is Gln, Arg, Val or Ile; Xaa at position 32 is Leu, Ala, Asn or Arg; Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe, 30 Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at position 45 is Gln, Val, or Met; Xaa at position 46 is Asp or Ser; Xaa at position 49 is Met, Ile, Leu or Asp; Xaa at position 50 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at 35 position 55 is Arg, Leu, or Thr; Xaa at position 56 is Pro

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or Ser; Xaa at position 59 is Glu or Leu; Xaa at position 60 is Ala or Ser; Xaa at position 62 is Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, His or Gln; Xaa at position 5 69 is Gln or Glu; Xaa at position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at position 79 is Lys, Arg or Ser; Xaa at position 82 is Leu, Glu, Val or Trp; Xaa at position 85 is Leu or Val; Xaa at position 87 is Leu, Ser, Tyr; Xaa at position 88 is Ala or Trp; Xaa at position 10 91 is Ala or Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or Thr; Xaa at position 98 is His, Ile, or Thr; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at position 105 is Asn or Glu; Xaa at position 109 is Arg, Glu or Leu; Xaa at position 112 15 is Thr or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; Xaa at position 117 is Thr or Ser; Xaa at position 120 is Asn, Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino 20 acids of native human interleukin-3.

12. The fusion protein of claim 11 wherein R₁ is of the formula:

25 1 5 10
(Met_m-Alan)p-Asn Cys Ser Xaa Xaa Xaa Asp Glu Xaa Ile
 15 20
Xaa His Leu Lys Xaa Pro Pro Xaa Pro Xaa Leu Asp Xaa

30 25 30 35
Xaa Asn Leu Asn Xaa Glu Asp Xaa Xaa Ile Leu Xaa Glu
 40 45
Xaa Asn Leu Arg Xaa Xaa Asn Leu Xaa Xaa Phe Xaa Xaa
 50 55 60
35 Ala Xaa Lys Xaa Leu Xaa Asn Ala Ser Xaa Ile Glu Xaa

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	65	70	75
	80	85	
	Ile Leu Xaa Asn Xaa Xaa Pro Cys Xaa Pro Xaa Ala Thr		
	Aia Xaa Pro Xaa Arg Xaa Pro Ile Xaa Ile Xaa Xaa Gly		
5	90	95	100
	Asp Trp Xaa Glu Phe Arg Xaa Lys Leu Xaa Phe Tyr Leu		
	105	110	
	Xaa Xaa Leu Glu Xaa Ala Gln Xaa Gln Gln [SEQ ID NO:8]		

10 wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile; Xaa at position 6 is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xaa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Ile; Xaa at position 18 is 15 Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile or Asp; Xaa at 20 position 36 is Glu or Asp; Xaa at position 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala or Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is 25 Val or Ser; Xaa at position 53 is Ser, Asn, His or Gln; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or Trp; Xaa at 30 position 71 is Leu or Val; Xaa at position 73 is Leu, Ser or Tyr; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87

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is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95 is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His;
5 Xaa at position 109 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125)human interleukin-3.

10 13. The fusion protein of claim 12 wherein R₁ is of the Formula:

15 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
20 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Gln [SEQ ID NO:9];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
25 Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
30 Leu Glu Asn Ala Gln Gln [SEQ ID NO:10];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
35 Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser

Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Gln Gln [SEQ ID NO:11];

5

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
10 Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Gln [SEQ ID NO:12];

15 Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
20 Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Gln [SEQ ID NO:13];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
25 Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
30 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Gln [SEQ ID NO:14];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly

Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
5 Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Gln [SEQ ID NO:15];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Asp Phe Asn Asn Leu Asn Gly
10 Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
15 Leu Glu Asn Ala Gln Gln [SEQ ID NO:16];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
20 Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:17];

25 Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
30 Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln [SEQ ID NO:18];

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
5. Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:19];

10 Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
15 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:20];

20 Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
25 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:21];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
30 Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr

Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:22];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
5 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
10 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:23];

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
15 Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:24];
20

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
25 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:25];

30 Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser

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Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:26];

5 Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
10 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:27];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
15 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
20 Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:28];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
25 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
30 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:29];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn

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Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
5 Leu Glu Asn Ala Gln Ala Gln Gln [SEQ ID NO:30];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
10 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:31];

15 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
20 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:32];

25 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
30 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:33];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu

Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
5 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:34];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
10 Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
15 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:35];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
20 Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
25 Leu Glu His Ala Gln Glu Gln [SEQ ID NO:36];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
30 Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln [SEQ ID NO:37];

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
5 Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:38];
10

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
15 Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln [SEQ ID NO:39].
20

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Ser Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
25 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:40]
30 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His Leu
Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
35 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:41]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
5 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
10 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:42]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
15 Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
20 Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:43]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
25 Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
30 Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:44]

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp

435

Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
5 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln [SEQ ID NO:45]

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
10 Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val
Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
15 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln
Ala Gln Glu Gln Gln
[SEQ ID NO:46]

20 Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu
25 Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln
Ala Gln Glu Gln Gln
[SEQ ID NO:47] and

30 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His Leu
Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser
Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser

Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:48].

5

14. The fusion protein of claim 13, wherein R1
is of the Formula:

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
10 Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
15 Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln [SEQ ID NO:30].

16. The fusion protein of claims
1,2,3,4,5,6,7,8,9,10,11,12, 13, or 14 wherein said colony
20 stimulating factor is G-CSF or GM-CSF.

17. The fusion protein of claim 1 selected from
group consisting of amino acid sequences corresponding to
SEQ. ID. NO: 121-159 and 165-168.

25

18. The fusion protein of claim 1 selected from
group consisting of amino acid sequences corresponding to
SEQ. ID. NO: 133,124,154 and 155.

30

19. A pharmaceutical composition comprising a
therapeutically effective amount of the fusion protein of
claims 1,2,3,4,5,6,7,8,9,10,11,12,13,14,16 or 17 and a
pharmaceutically acceptable carrier.

19. A pharmaceutical composition comprising a therapeutically effective amount of the fusion protein of claim 15 and a pharmaceutically acceptable carrier.

5

20. A method of increasing hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of the fusion protein of claims 1,2,3,4,5,6,7,8,9,10,11,12,13,14,16
10 or 17.

21. A method of increasing hematopoietic cell production in a mammal in need thereof comprising administering a pharmaceutically effective amount of the
15 fusion protein of claim 15.

22. Recombinant DNA comprising vector DNA and DNA that encodes for a polypeptide selected from group consisting of nucleotide sequences corresponding to SEQ. ID.
20 NO: 53-90 and 183-186.

23. A recombinant DNA of claim 22 selected from group consisting of nucleotide sequences corresponding to SEQ. ID. NO: 60,64,89 and 98,
25

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1 5 10
ATG GCT CCA ATG ACT CAG ACT ACT TGT CCT AAG ACT TCT
Met Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser

15 20 25
TGG GTT AAC TGC TCT AAC ATG ATC GAT GAA ATT ATA ACA
Trp Val Asn Cys Ser Asn Met Ile Asp Glu Ile Thr Thr

30 35
CAC TTA AAG CAG CCA CCT TTG CCT TTG CTG GAC TTC AAC
His Leu Lys Gln Pro Pro Leu Pro Leu Asp Phe Asn

40 45 50
AAC CTC AAT GGG GAA GAC CAA GAC ATT CTG ATG GAA AAT
Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn

55 60
AAC CTT CGA AGG CCA AAC CTG GAG GCA TTC AAC AGG GCT
Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala

65 70 75
GTC AAG AGT TTA CAG AAT GCA TCA GCA ATT GAG AGC ATT
Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile

80 85 90
CTT AAA AAT CTC CTG CCA TGT CTG CCC CTG GCC ACG GCC
Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala

95 100
GCA CCC ACG CGA CAT CCA ATC CAT ATC AAG GAC GGT GAC
Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp

105 110 115
TGG AAT GAA TTC CGT CGT AAA CTG ACC TTC TAT CTG AAA
Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys

120 125
ACC TTG GAG AAC GGG CAG CCT CAA CAG ACC ACT CTG TCG
Thr Leu Glu Asn Ala Gln Ala Gln Thr Thr Leu Ser

130
CTA GCG ATC TTT TAA TAA [SEQ ID NO:144]
Leu Ala Ile Phe END END [SEQ ID NO:128]

FIG. 1

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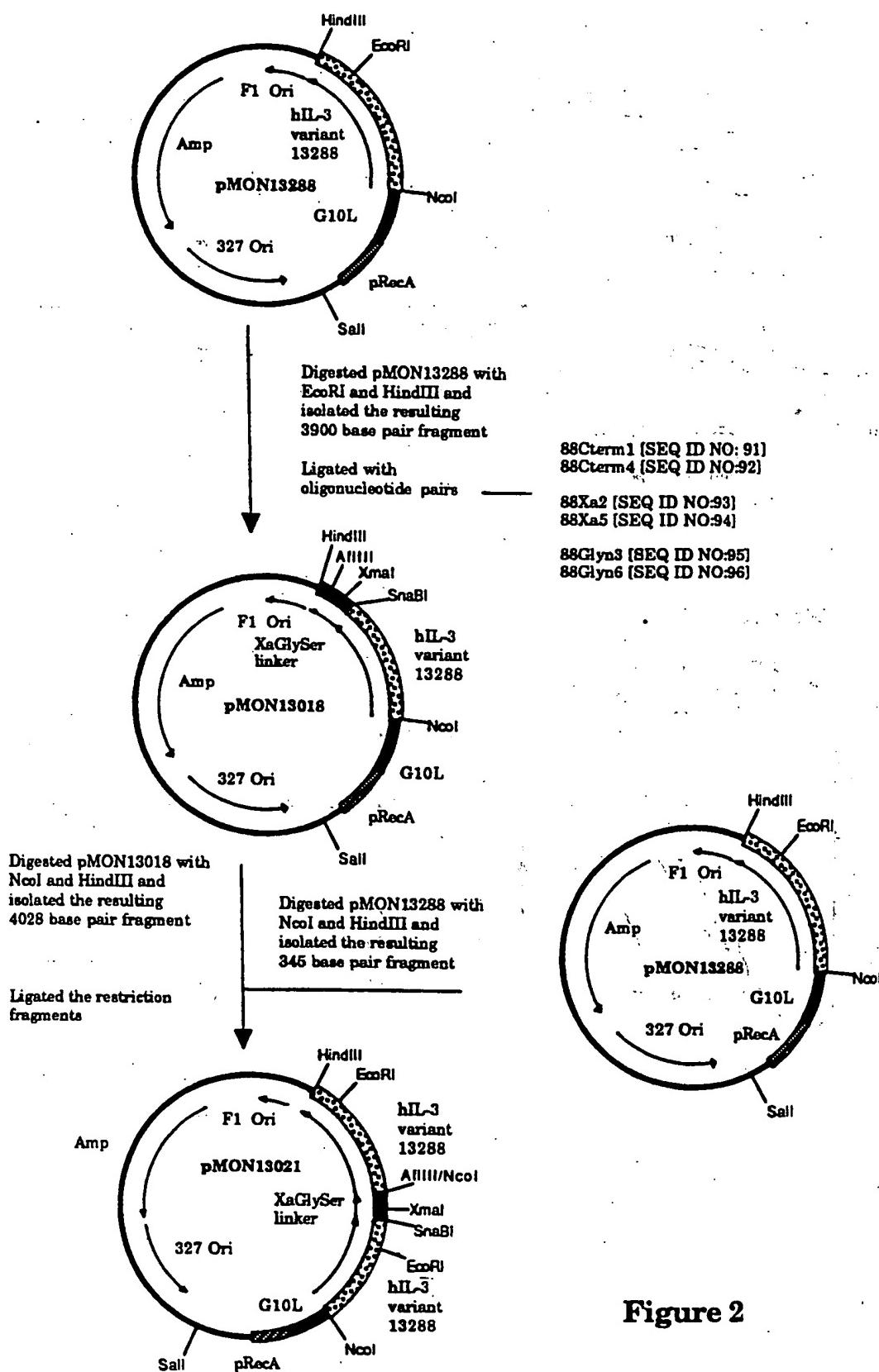


Figure 2

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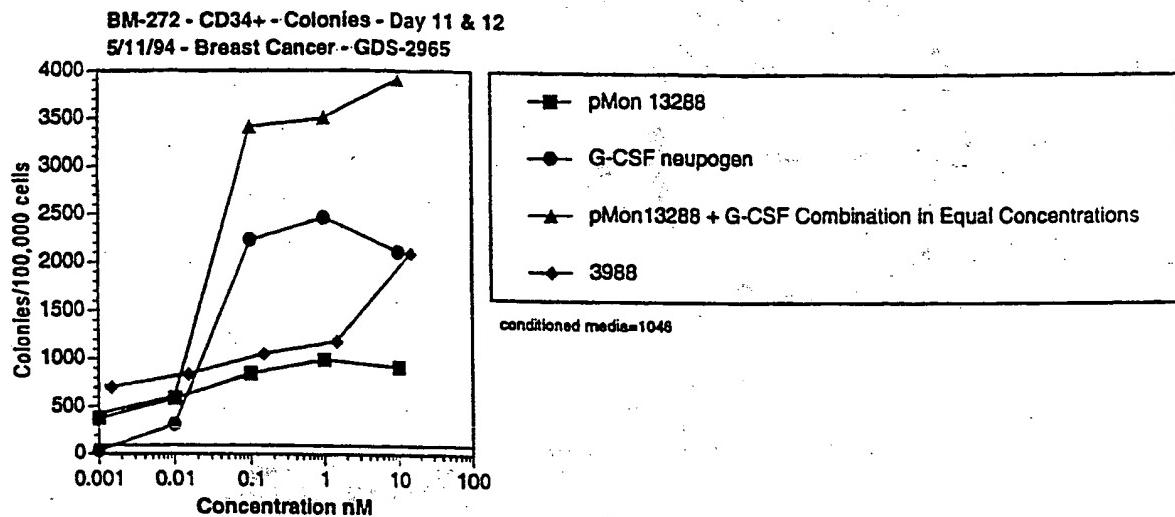
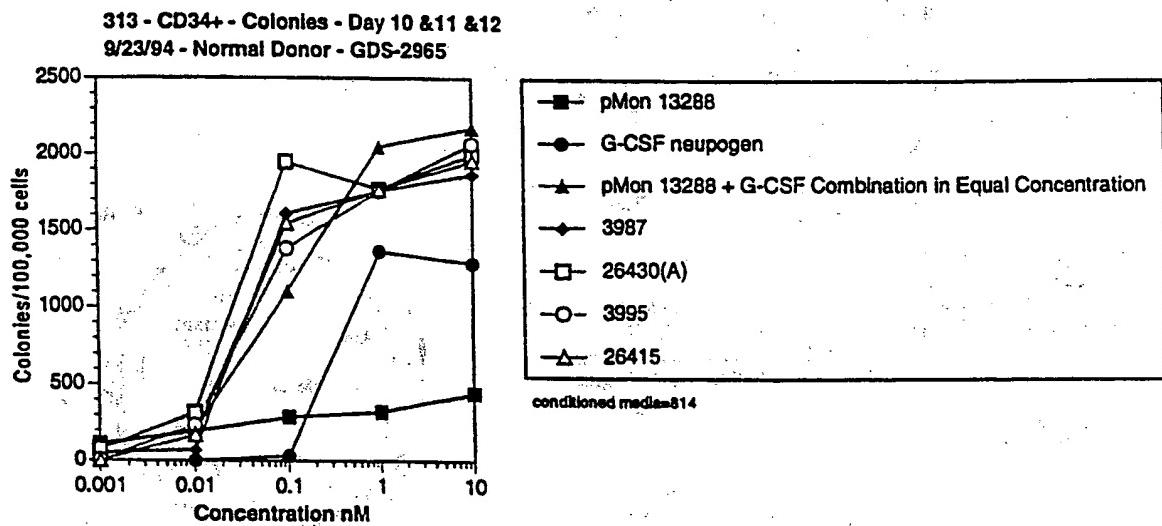
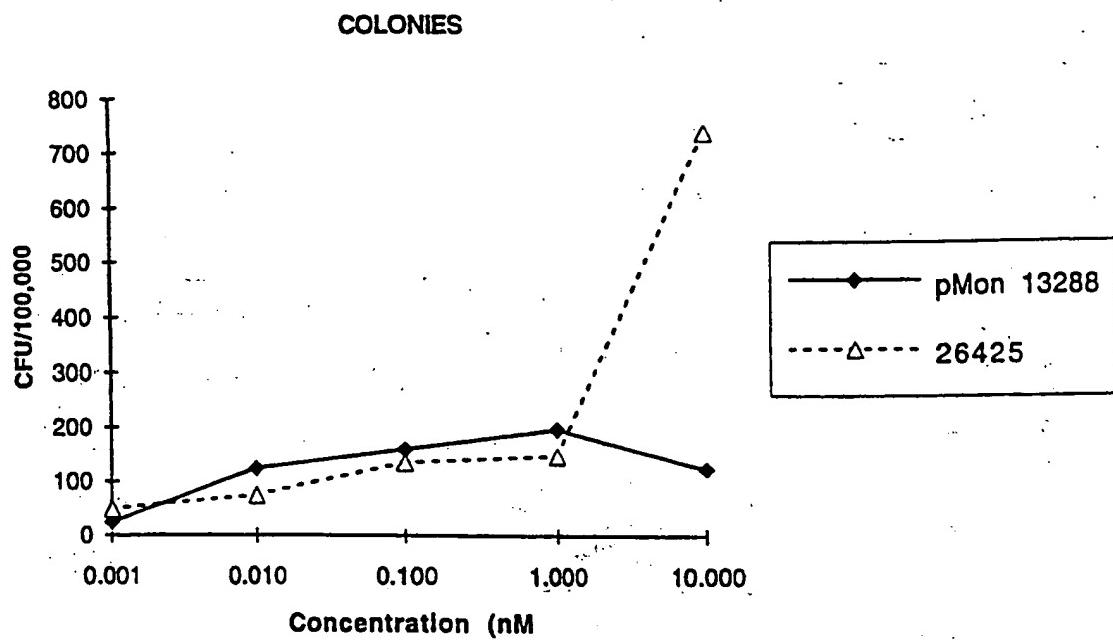
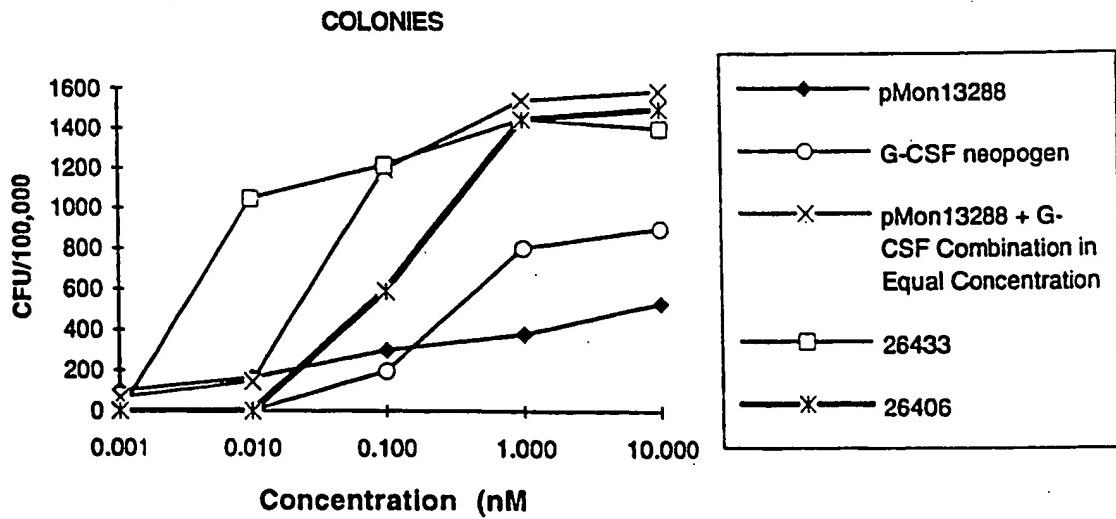
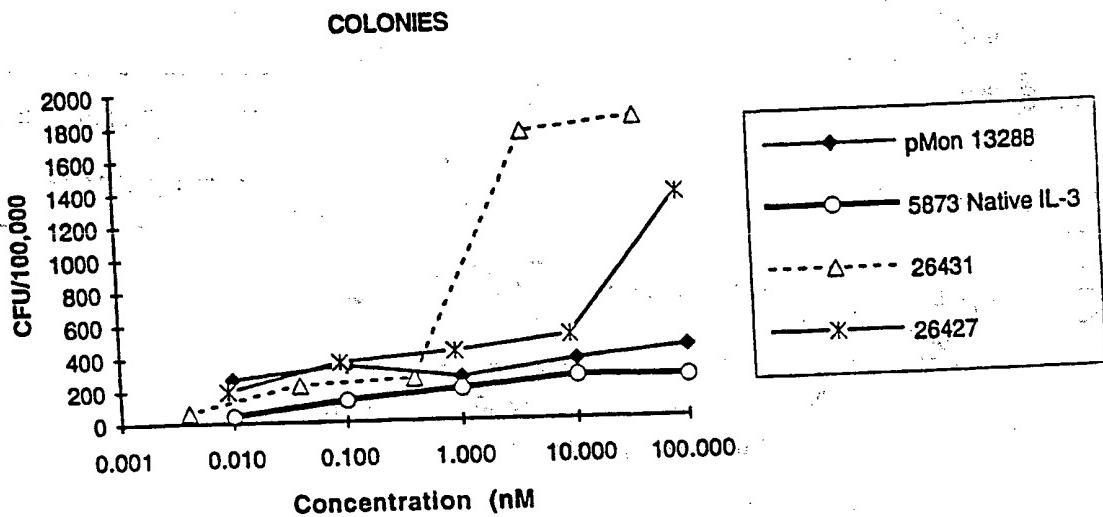
Figure 3**Figure 4**

Figure 5

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**Figure 6**

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Figure 7

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 95/01185

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/24 C07K19/00 C07K14/54 A61K38/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,91 02754 (IMMUNEX CORPORATION) 7 March 1991 cited in the application see the whole document ---	1-23
Y	WO,A,92 06116 (ORTHO PHARMACEUTICAL CORPORATION) 16 April 1992 see the whole document ---	1-23
Y	WO,A,92 04455 (GENETICS INSTITUTE) 19 March 1992 cited in the application see the whole document ---	1-23
P,Y	WO,A,94 12638 (SEARLE) 9 June 1994 see the whole document -----	1-23

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

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Date of the actual completion of the international search

2 June 1995

Date of mailing of the international search report

19 -06- 1995

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.

Authorized officer

Moreau, J

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US95/01185

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Remark : Although claims 20-21 are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 95/01185

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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		DE-D-	69007975	11-05-94
		DE-T-	69007975	21-07-94
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		JP-T-	5502463	28-04-93
		ZA-A-	9107766	29-03-93
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		AU-A-	8917491	30-03-92
		CA-A-	2089553	01-03-92
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		WO-A-	9412639	09-06-94
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